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(71) Applicant: ASSOCIATED UNIVERSITIES, INC. [US/US]; Suite 730, 1400 16th Street N.W., Washington, DC 20036

(US).

(72) Inventors: DUNN, John, J.; 5 Mott Drive, Bellport, NY 11713 (US). LUFT, Benjamin, J.; 223 Lincoln Avenue, Port

Jefferson, NY 11777 (US).

(74) Agents: GRANAHAN, Patricia et al.; Hamilton, Brook, Smith & Reynolds, Two Militia Drive, Lexington, MA 02173 ·(US).

(54) Title: CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: USES THEREFOR

#### (57) Abstract

Novel chimeric nucleic acids, encoding chimeric Borrelia proteins consisting of at least two antigenic polypeptides from corresponding and/or non-corresponding proteins from the same and/or different species of Borrelia, are disclosed. Chimeric proteins encoded by the nucleic acid sequences are also disclosed. The chimeric proteins are useful as vaccine immunogens against Lyme borreliosis, as well as for immunodiagnostic reagents.

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## CHIMERIC PROTEINS COMPRISING BORRELIA POLYPEPTIDES: <u>USES THEREFOR</u>

### Background of the Invention

- Lyme borreliosis is the most common tick-borne
  infectious disease in North America, Europe, and
  northern Asia. The causative bacterial agent of this
  disease, Borrelia burgdorferi, was first isolated and
  cultivated in 1982 (Burgdorferi, W.A. et al., Science
  216: 1317-1319 (1982); Steere, A.R. et al., N. Engl. J.
- Med. 308: 733-740 (1983)). With that discovery, a wide array of clinical syndromes, described in both the European and American literature since the early 20th century, could be attributed to infection by B. burgdorferi (Afzelius, A., Acta Derm. Venereol. 2: 120-
- 15 125 (1921); Bannwarth, A., Arch. Psychiatr.
   Nervenkrankh. 117: 161-185 (1944); Garin, C. and A.
  Bujadouz, J. Med. Lyon 71: 765-767 (1922); Herxheimer,
   K. and K. Hartmann, Arch. Dermatol. Syphilol. 61: 57-76,
   255-300 (1902)).
- The immune response to B. burgdorferi is characterized by an early, prominent, and persistent humoral response to the end of lagellar protein, p41 (fla), and to a protein constituent of the protoplasmic cylinder, p93 (Szczepanski, A., and J.L. Benach,
- Microbiol. Rev. 55:21 (1991)). The p41 flagellin antigen is an immunodominant protein; however, it shares significant homology with flagellins of other microorganisms and therefore is highly cross reactive. The p93 antigen is the largest immunodominant antigen of
- 30 B. burgdorferi. Both the p41 and p93 proteins are physically cryptic antigens, sheathed from the immune system by an outer membrane whose major protein constituents are the outer surface proteins A and B

(OspA and OspB). OspA is a basic lipoprotein of approximately 31 kd, which is encoded on a large linear plasmid along with OspB, a basic lipoprotein of approximately 34 kd (Szczepanski, A., and J.L. Benach, Microbiol. Rev. 55:21 (1991)). Analysis of isolates of B. burgdorferi obtained from North America and Europe has demonstrated that OspA has antigenic variability, and that several distinct groups can be serologically and genotypically defined (Wilske, B., et al., World J. Microbiol. 7: 130 (1991)). Other Borrelia proteins 10 demonstrate similar antigenic variability. Surprisingly, the immune response to these outer surface proteins tends to occur late in the disease, if at all (Craft, J. E. et al., <u>J. Clin Invest. 78</u>: 934-939 (1986); Dattwyler, R.J. and B.J. Luft, Rheum. Clin. 15 North Am. 15: 727-734 (1989)). Furthermore, patients acutely and chronically infected with B. burgdorferi respond variably to the different antigens, including OspA, OspB, OspC, OspD, p39, p41 and p93. Vaccines against Lyme borreliosis have been 20

Vaccines against Lyme borreliosis have been attempted. Mice immunized with a recombinant form of OspA are protected from challenge with the same strain of B. burgdorferi from which the protein was obtained (Fikrig, E., et al., Science 250: 553-556 (1990)).

Furthermore, passively transferred anti-OspA monoclonal antibodies (Mabs) have been shown to be protective in mice, and vaccination with a recombinant protein induced protective immunity against subsequent infection with the homologous strain of B.burgdorferi (Simon, M.M., et

al., <u>J. Infect. Dis. 164</u>: 123 (1991)). Unfortunately, immunization with a protein from one strain does not necessarily confer resistance to a heterologous strain (Fikrig, E. et al., <u>J. Immunol. 7</u>: 2256-1160 (1992)), but rather, is limited to the homologous 'species' from which the protein was prepared. Furthermore,

immunization with a single protein from a particular strain of Borrelia will not confer resistance to that strain in all individuals. There is considerable variation displayed in OspA and OspB, as well as p93, including the regions conferring antigenicity.

Therefore, the degree and frequency of protection from vaccination with a protein from a single strain depend upon the response of the immune system to the particular variation, as well as the frequency of genetic variation in B. burgdorferi. Currently, a need exists for a vaccine which provides immunogenicity across species and to more epitopes within a species, as well as immunogenicity against more than one protein.

### Summary of the Invention

The current invention pertains to chimeric Borrelia proteins which include two or more antigenic Borrelia polypeptides which do not occur naturally (in nature) in the same protein in Borrelia, as well as the nucleic acids encoding such chimeric proteins. The antigenic polypeptides incorporated in the chimeric proteins are derived from any Borrelia protein from any strain of Borrelia, and include outer surface protein (Osp) A, OspB, OspC, OspD, p12, p39, p41, p66, and p93. proteins from which the antigenic polypeptides are 25 derived can be from the same strain of Borrelia, from different strains, or from combinations of proteins from the same and from different strains. If the proteins from which the antigenic polypeptides are derived are OspA or OspB, the antigenic polypeptides can be derived 30 from either the portion of the OspA or OspB protein present between the amino terminus and the conserved tryptophan of the protein (referred to as a proximal portion), or the portion of the OspA or OspB protein present between the conserved tryptophan of the protein

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and the carboxy terminus (referred to as a distal portion). Particular chimeric proteins, and the nucleotide sequences encoding them, are set forth in Figures 23-37 and 43-46.

The chimeric proteins of the current invention provide antigenic polypeptides of a variety of Borrelia strains and/or proteins within a single protein. Such proteins are particularly useful in immunodiagostic assays to detect the presence of antibodies to native Borrelia in potentially infected individuals as well as to measure T-cell reactivity, and can therefore be used as immunodiagnostic reagents. The chimeric proteins of the current invention are additionally useful as vaccine immunogens against Borrelia infection.

For a better understanding of the present invention together with other and further objects, reference is made to the following description, taken together with the accompanying drawings.

### Brief Description of the Drawings

Figure 1 summarizes peptides and antigenic domains localized by proteolytic and chemical fragmentation of OspA.

Figure 2 is a comparison of the antigenic domains depicted in Figure 1, for OspA in nine strains of B. burgdorferi.

Figure 3 is a graph depicting a plot of weighted polymorphism versus amino acid position among 14 OspA variants. The marked peaks are: a) amino acids 132-145; b) amino acids 163-177; c) amino acids 208-221. The lower dotted line at polymorphism value 1.395 demarcates statistically significant excesses of polymorphism at p = 0.05. The upper dotted line at 1.520 is the same, except that the first 29 amino acids at the monomorphic N-terminus have been removed from the original analysis.

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Figure 4 depicts the amino acid alignment of residues 200 through 220 for OspAs from strains B31 and K48 as well as for the site-directed mutants 613, 625, 640, 613/625, and 613/640. Arrow indicates Trp216.

5 Amino acid changes are underlined.

Figure 5 is a helical wheel projection of residues 204-217 of B31 OspA. Capital letters indicate hydrophobic residues; lower case letters indicate hydrophilic residues; +/- indicate positively/negatively charged residues. Dashed line indicates division of the alpha-helix into hydrophobic arc (above the line) and polar arc (below the line). Adapted from France et al. (Biochem. Biophys. Acta 1120: 59 (1992)).

Figure 6 depicts a phylogenic tree for strains of Borrelia described in Table I. The strains are as follows: 1 = B31; 2 = Pka1; 3 = ZS7; 4 = N40; 5 = 25015; 6 = K48; 7 = DK29; 8 = PHei; 9 = Ip90; 10 = PTrob; 11 = ACAI; 12 = PGau; 13 = Ip3; 14 = PBo; 15 = PKo.

Figure 7 depicts the nucleic acid sequence of OspA-B31 (SEW ID NO. 6), and the encoded protein sequence (SEQ ID NO. 7).

Figure 8 depicts the nucleic acid sequence of OspA-K48 (SEQ ID NO. 8), and the encoded protein sequence (SEQ ID NO. 9).

Figure 9 depicts the nucleic acid sequence of OspA-PGau (SEQ ID NO. 10), and the encoded protein sequence (SEQ ID NO. 11).

Figure 10 depicts the nucleic acid sequence of 30 OspA-25015 (SEQ ID NO. 12), and the encoded protein sequence (SEQ ID NO. 13).

Figure 11 depicts the nucleic acid sequence of OspB-B31 (SEQ ID NO. 21), and the encoded protein sequence (SEQ ID NO. 22).

Figure 12 depicts the nucleic acid sequence of OspC-B31 (SEQ ID NO. 29), and the encoded protein sequence (SEQ ID NO. 30).

Figure 13 depicts the nucleic acid sequence of OspC-K48 (SEQ ID NO. 31), and the encoded protein sequence (SEQ ID NO. 32).

Figure 14 depicts the nucleic acid sequence of OspC-PKo (SEQ ID NO. 33), and the encoded protein sequence (SEQ ID NO. 34).

10 Figure 15 depicts the nucleic acid sequence of OspC-pTrob (SEQ ID NO. 35) and the encoded protein sequence (SEQ ID NO. 36).

Figure 16 depicts the nucleic acid sequence of p93-B31 (SEQ ID NO. 65) and the encoded protein sequence (SEQ ID NO. 66).

Figure 17 depicts the nucleic acid sequence of p93-K48 (SEQ ID NO. 67).

Figure 18 depicts the nucleic acid sequence of p93-PBo (SEQ ID NO. 69).

20 Figure 19 depicts the nucleic acid sequence of p93-pTrob (SEQ ID NO. 71).

Figure 20 depicts the nucleic acid sequence of p93-pGau (SEQ ID NO. 73).

Figure 21 depicts the nucleic acid sequence of p93-25 25015 (SEQ ID NO. 75).

Figure 22 depicts the nucleic acid sequence of p93pKo (SEQ ID NO. 77).

Figure 23 depicts the nucleic acid sequence of the OspA-K48/OspA-PGau chimer (SEQ ID NO. 85) and the encoded chimeric protein sequence (SEQ ID NO. 86).

Figure 24 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau chimer (SEQ ID NO. 88) and the encoded chimeric protein sequence (SEQ ID NO. 89).

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Figure 25 depicts the nucleic acid sequence of the OspA-B31/OspA-K48 chimer (SEQ ID NO. 91) and the encoded chimeric protein sequence (SEQ ID NO. 92).

Figure 26 depicts the nucleic acid sequence of the OspA-B31/OspA-25015 chimer (SEQ ID NO. 94) and the encoded chimeric protein sequence (SEQ ID NO. 95).

Figure 27 depicts the nucleic acid sequence of the OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 97) and the encoded chimeric protein sequence (SEQ ID NO. 98).

Figure 28 depicts the nucleic acid sequence of the OspA-B31/OspA-K48/OspA-B31/OspA-K48 chimer (SEQ ID NO. 100) and the encoded chimeric protein sequence (SEQ ID NO. 101).

Figure 29 depicts the nucleic acid sequence of the OspA-B31/OspB-B31 chimer (SEQ ID NO. 103) and the encoded chimeric protein sequence (SEQ ID NO. 104).

Figure 30 depicts the nucleic acid sequence of the OspA-B31/OspB-B31/OspC-B31 chimer (SEQ ID NO. 106) and the encoded chimeric protein sequence (SEQ ID NO. 107).

Figure 31 depicts the nucleic acid sequence of the OspC-B31/OspA-B31/OspB-B31 chimer (SEQ ID NO. 109) and the encoded chimeric protein sequence (SEQ ID NO. 110).

Figure 32 depicts the nucleic acid sequence of the OspA-B31/p93-B31 chimer (SEQ ID NO. 111) and the encoded chimeric protein sequence (SEQ ID NO. 112).

Figure 33 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234) chimer (SEQ ID NO. 113) and the encoded chimeric protein sequence (SEQ ID NO. 114).

Figure 34 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-295) chimer (SEQ ID NO. 115) and the encoded chimeric protein sequence (SEQ ID NO. 116).

Figure 35 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-234) chimer (SEQ ID NO. 117) and the encoded chimeric protein sequence (SEQ ID NO. 118).

Figure 36 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (140-295) chimer (SEQ ID NO. 119) and the encoded chimeric protein sequence (SEQ ID NO. 120).

Figure 37 depicts the nucleic acid sequence of the OspB-B31/p41-B31 (122-234)/OspC-B31 chimer (SEQ ID NO. 121) and the encoded chimeric protein sequence (SEQ ID NO. 122).

Figure 38 depicts an alignment of the nucleic acid sequences for OspC-B31 (SEQ ID NO. 29), OspC-PKo (SEQ ID NO. 33), OspC-pTrob (SEQ ID NO. 35), and OspC-K48 (SEQ ID NO. 31). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspC-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 39 depicts an alignment of the nucleic acid sequences for OspD-pBO (SEQ ID NO. 123), OspD-PGau (SEQ ID NO. 124), OspD-DK29 (SEQ ID NO. 125), and OspD-K48 (SEQ ID NO. 126). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspD-pBo) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 40 depicts the nucleic acid sequence of p41-B31 (SEq ID NO. 127) and then encoded protein sequence (SEQ ID NO. 128).

Figure 41 depicts an alignment of the nucleic acid sequences for p41-B31 (SEQ ID NO. 127), p41-pKa1 (SEQ ID NO. 129), p41-PGau (SEQ ID NO. 51), p41-PBo (SEQ ID NO. 130), p41-DK29 (SEQ ID NO. 53), and p41-PKo (SEQ ID NO. 131). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, p41-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

Figure 42 depicts an alignment of the nucleic acid sequences for OspA-B31 (SEQ ID NO. 6), OspA-pKal (SEQ ID NO. 132), OspA-N40 (SEQ ID NO. 133), OspA-ZS7 (SEQ ID

NO. 134), OspA-25015 (SEQ ID NO. 12), OspA-pTrob (SEQ ID NO. 135), OspA-K48 (SEQ ID NO. 8), OspA-Hei (SEQ ID NO. 136), OspA-DK29 (SEQ ID NO. 49), OspA-Ip90 (SEQ ID NO. 50), OspA-pBo (Seq ID NO. 55), OspA-Ip3 (SEQ ID NO. 56), OspA-PKo (SEQ ID NO. 57), OspA-ACAI (SEQ ID NO. 58), and OspA-PGau (SEQ ID NO. 10). Nucleic acids which are identical to those in the lead nucleic acid sequence (here, OspA-B31) are represented by a period (.); differing nucleic acids are shown in lower case letters.

10 Figure 43 depicts the nucleic acid sequence of the OspA-Tro/OspA-Bo chimer (SEQ ID NO. 137) and the encoded chimeric protein sequence (SEQ ID NO. 138).

Figure 44 depicts the nucleic acid sequence of the OspA-PGau/OspA-Bo chimer (SEQ ID NO. 139) and the encoded chimeric protein sequence (SEQ ID NO. 140).

Figure 45 depicts the nucleic acid sequence of the OspA-B31/OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 141) and the encoded chimeric protein sequence (SEQ ID NO. 142).

Figure 46 depicts the nucleic acid sequence of the OspA-PGau/OspA-B31/OspA-K48 chimer (SEQ ID NO. 143) and the encoded chimeric protein sequence (SEQ ID NO. 144).

### Detailed Description of the Invention

The current invention pertains to chimeric proteins
comprising antigenic Borrelia polypeptides which do not
occur in nature in the same Borrelia protein. The
chimeric proteins are a combination of two or more
antigenic polypeptides derived from Borrelia proteins.
The antigenic polypeptides can be derived from different
proteins from the same species of Borrelia, or different
proteins from different Borrelia species, as well as
from corresponding proteins from different species. As
used herein, the term "chimeric protein" describes a
protein comprising two or more polypeptides which are

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derived from corresponding and/or non-corresponding native Borrelia protein. A polypeptide "derived from" a native Borrelia protein is a polypeptide which has an amino acid sequence the same as an amino acid sequence present in a Borrelia protein, an amino acid sequence equivalent to the amino acid sequence of a naturally occurring Borrelia protein, or an amino acid sequence substantially similar to the amino acid sequence of a naturally occurring Borrelia protein (e.g., differing by few amino acids) such as when a nucleic acid encoding a protein is subjected to site-directed mutagenesis. "Corresponding" proteins are equivalent proteins from different species or strains of Borrelia, such as outer surface protein A (OspA) from strain B31 and OspA from strain K48. The invention additionally pertains to nucleic acids encoding these chimeric proteins.

As described below, Applicants have identified two separate antigenic domains of OspA and OspB which flank the sole conserved tryptophan present in OspA and in These domains share cross-reactivity with different genospecies of Borrelia. The precise amino acids responsible for antigenic variability were determined through site-directed mutagenesis, so that proteins with specific amino acid substitutions are available for the development of chimeric proteins. Furthermore, Applicants have identified immunologically important hypervariable domains in OspA proteins, as described below in Example 2. The first hypervariable domain of interest for chimeric proteins, Domain A, 30 includes amino acid residues 120-140 of OspA, the second hypervariable domain, Domain B, includes residues 150-180 and the third hypervariable domain, Domain C, includes residues 200-216 or 217 (depending on the position of the sole conserved tryptophan residue in the OspA of that particular species of Borrelia) (see Figure 3). In addition, Applicants have sequenced the genes for several *Borrelia* proteins.

These discoveries have aided in the development of novel recombinant Borrelia proteins which include two or more amino acid regions or sequences which do not occur in the same Borrelia protein in nature. The recombinant proteins comprise polypeptides from a variety of Borrelia proteins, including, but not limited to, OspA, OspB, OspC, OspD, p12, p39, p41, p66, and p93.

10 Antigenically relevant polypeptides from each of a number of proteins are combined into a single chimeric protein.

In one embodiment of the current invention, chimers are now available which include antigenic polypeptides 15y flanking a tryptophan residue. The antigenic polypeptides are derived from either the proximal portion from the tryptophan (the portion of the OspA or cospB protein present between the amino terminus and the conserved tryptophan of the protein), or the distal portion from the tryptophan (the portion of the OspA or OspB protein present between the conserved tryptophan of the protein and the carboxy terminus) in OspA and/or The resultant chimers can be OspA-OspA chimers (i.e., chimers incorporating polypeptides derived from 25 OspA from different strains of Borrelia), OspA-OspB chimers, or OspB-OspB chimers, and are constructed such that amino acid residues amino-proximal to an invariant tryptophan are from one protein and residues carboxyproximal to the invariant tryptophan are from the other protein. For example, one available chimer consists of a polypeptide derived from the amino-proximal region of OspA from strain B31, followed by the tryptophan residue, followed by a polypeptide derived from the carboxy-proximal region of OspA from strain K48 (SEQ ID

35 NO. 92). Another available chimer includes a

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polypeptide derived from the amino-proximal region of OspA from strain B31, and a polypeptide derived from the carboxy-proximal region of OspB from strain B31 (SEQ ID NO. 104). If the polypeptide proximal to the tryptophan 5 of these chimeric proteins is derived from OspA, the proximal polypeptide can be further subdivided into the three hypervariable domains (Domains A, B, and C), each of which can be derived from OspA from a different strain of Borrelia. These chimeric proteins can further comprise antigenic polypeptides from another protein, in addition to the antigenic polypeptides flanking the tryptophan residue.

In another embodiment of the current invention, chimeric proteins are available which incorporate antigenic domains of two or more Borrelia proteins, such as Osp proteins (Osp A, B, C and/or D) as well as p12, p39, p41, p66, and/or p93.

The chimers described herein can be produced so that they are highly soluble, hyper-produced in E. coli, and non-lipidated. In addition, the chimeric proteins can be designed to end in an affinity tag (His-tag) to facilitate purification. The recombinant proteins described herein have been constructed to maintain high levels of antigenicity. In addition, recombinant proteins specific for the various genospecies of Borrelia that cause Lyme disease are now available, because the genes from each of the major genospecies have been sequenced; the sequences are set forth below. These recombinant proteins with their novel biophysical and antigenic properties will be important diagnostic reagent and vaccine candidates.

The chimeric proteins of the current invention are advantageous in that they retain specific reactivity to monoclonal and polyclonal antibodies against wild-type Borrelia proteins, are immunogenic, and inhibit the

growth or induce lysis of Borrelia in vitro.

Furthermore, in some embodiments, the proteins provide antigenic domains of two or more Borrelia strains and/or proteins within a single protein. Such proteins are

5 particularly useful in immuno-diagostic assays. For example, proteins of the present invention can be used as reagents in assays to detect the presence of antibodies to native Borrelia in potentially infected individuals. These proteins can also be used as

10 immunodiagnostic reagents, such as in dot blots, Western blots, enzyme linked immunosorbed assays, or agglutination assays. The chimeric proteins of the present invention can be produced by known techniques, such as by recombinant methodology, polymerase chain

15 reaction, or mutagenesis.

Furthermore, the proteins of the current invention are useful as vaccine immunogens against Borrelia infection. Because Borrelia has been shown to be clonal, a protein comprising antigenic polypeptides from 20 a variety of Borrelia proteins and/or species, will provide immunoprotection for a considerable time when used in a vaccine. The lack of significant intragenic recombination, a process which might rapidly generate novel epitopes with changed antigenic properties, 25 ensures that Borrelia can only change antigenic type by accumulating mutational change, which is slow when compared with recombination in generating different antigenic types. The chimeric protein can be combined with a physiologically acceptable carrier and 30 administered to a vertebrate animal through standard methods (e.g., intravenously or intramuscularly, for example).

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The current invention is illustrated by the following Examples, which are not to be construed to be limiting in any way.

# Example 1. Purification of Borrelia burgorferi Outer Surface Protein A and Analysis of Antibody Binding Domains

This example details a method for the purification of large amounts of native outer surface protein A (OspA) to homogeneity, and describes mapping of the antigenic specificities of several anti-OspA MAbs. OspA was purified to homogeneity by exploiting its resistance to trypsin digestion. Intrinsic labeling with <sup>14</sup>C-palmitic acid confirmed that OspA was lipidated, and partial digestion established lipidation at the aminoterminal cysteine of the molecule.

The reactivity of seven anti-OspA murine monoclonal antibodies to nine different Borrelia isolates was ascertained by Western blot analysis. Purified OspA was fragmented by enzymatic or chemical cleavage, and the monoclonal antibodies were able to define four distinct immunogenic domains (see Figure 1). Domain 3, which included residues 190-220 of OspA, was reactive with protective antibodies known to agglutinate the organism in vitro, and included distinct specificities, some of which were not restricted to a genotype of B. burgdorferi.

### A. Purification of Native OspA

Detergent solubilization of B. burgdorferi strips the outer surface proteins and yields partially-purified preparations containing both OspA and outer surface 5 protein B (Osp B) (Barbour, A.G. et al., Infect. Immun. 52 (5): 549-554 (1986); Coleman, J.L. and J.L. Benach, J <u>Infect. Dis. 155 (4)</u>: 756-765 (1987); Cunningham, T.M. et al., Ann. NY Acad. Sci. 539: 376-378 (1988); Brandt, M.E. et al., <u>Infect. Immun. 58</u>: 983-991 (1990); Sambri, 10 V. and R. Cevenini, Microbiol. 14:307-314 (1991)). Although both OspA and OspB are sensitive to proteinase K digestion, in contrast to OspB, OspA is resistant to cleavage by trypsin (Dunn, J. et al., Prot. Exp. Purif. 1: 159-168 (1990); Barbour, A.G. et al., Infect. Immun. 15 45:94-100 (1984)). The relative insensitivity to trypsin is surprising in view of the fact that Osp A has a high (16% for B31) lysine content, and may relate to the relative configuration of Osp A and B in the outer membrane.

Intrinsic Radiolabeling of Borrelia

Labeling for lipoproteins was performed as described by Brandt et al. (<u>Infect. Immun. 58</u>:983-991 (1990)). <sup>14</sup>C-palmitic acid (ICN, Irvine, California) was added to the BSK II media to a final concentration of 0.5 μCi per milliliter (ml). Organisms were cultured at 34°C in this medium until a density of 10<sup>8</sup> cells per ml was achieved.

Purification of OspA Protein from Borrelia Strain B31

Borrelia burgdorferi, either 14C-palmitic acidlabeled or unlabeled, were harvested and washed as
described (Brandt, M.E. et al., Infect. Immun. 58:983991 (1990)). Whole organisms were trypsinized according

to the protocol of Barbour et al. (Infect. Immun. 45:94-100 (1984)) with some modifications. The pellet was suspended in phosphate buffered saline (PBS, 10mM, pH 7.2), containing 0.8% tosyl-L-phenylalanine chloromethyl ketone (TPCK) -treated trypsin (Sigma, St. Louis, Missouri), the latter at a ratio of 1  $\mu$ g per 108 cells. Reaction was carried out at 25°C for 1 hour, following which the cells were centrifuged. The pellet was washed in PBS with 100  $\mu$ g/ml phenylmethylsulfonyl fluoride Triton X-114 partitioning of the pellet was -10 carried out as described by Brandt et al. (Infect. Immun. 58:983-991 (1990)). Following trypsin treatment, cells were resuspended in ice-cold 2% (v/v) Triton X-114 in PBS at 109 cells per ml. The suspension was rotated overnight at 4°C, and the insoluble fraction removed as a pellet after centrifugation at 10,000 X g for 15 minutes at 4°C. The supernatant (soluble fraction) was incubated at 37°C for 15 minutes and centrifuged at room temperature at 1000 X g for 15 minutes to separate the aqueous and detergent phases. The aqueous phase was decanted, and ice cold PBS added to the lower Triton phase, mixed, warmed to 37°C, and again centrifuged at 1000 X g for 15 minutes. Washing was repeated twice more. Finally, detergent was removed from the preparation using a spin column of Bio-beads SM2 25 (BioRad, Melville, New York) as described (Holloway, P.W., Anal. Biochem. 53:304-308 (1973)).

Ion exchange chromatography was carried out as described by Dunn et al. (Prot. Exp. Purif. 1: 159-168 (1990)) with minor modifications. Crude OspA was dissolved in buffer A (1% Triton X-100, 10mM phosphate buffer (pH 5.0)) and loaded onto a SP Sepharose resin (Pharmacia, Piscataway, New Jersey), pre-equilibrated with buffer A at 25°C. After washing the column with 10

bed-volumes of buffer A, the bound OspA was eluted with buffer B (1% Triton X-100, 10mM phosphate buffer (pH 8.0)). OspA fractions were detected by protein assay using the BCA method (Pierce, Rockford, Illinois), or as radioactivity when intrinsically labeled material was fractionated. Triton X-100 was removed using a spin column of Bio-beads SM2.

This method purifies OspA from an outer surface membrane preparation. In the absence of trypsin
10 treatment, OspA and B were the major components of the soluble fraction obtained after Triton partitioning of strain B31. In contrast, when Triton extraction was carried out after trypsin-treatment, the OspB band is not seen. Further purification of OspA-B31 on a SP

15 Sepharose column resulted in a single band by SDS-PAGE. The yield following removal of detergent was approximately 2 mg per liter of culture. This method of purification of OspA, as described herein for strain B31, can be used for other isolates of Borrelia as well.

20 For strains such as strain K48, which lack OspB, trypsin treatment can be omitted.

### Lipidation site of OspA-B31

purified as described above and partially digested with endoproteinase Asp-N (data not shown). Following digestion, a new band of lower molecular weight was apparent by SDS-PAGE, found by direct amino-terminal sequencing to begin at Asp<sub>2</sub>. This band had no trace of radioactivity by autoradiography (data not shown). OspA and B contain a signal sequence (L-X-Y-C) similar to the consensus described for lipoproteins of E. coli, and it has been predicted that the lipidation site of OspA and B should be the amino-terminal cysteine (Brandt, M.E. et

al., <u>Infect. Immun 58</u>: 983-991 (1990)). The results presented herein support this prediction.

## B. Comparison of OspA Antibody Binding Regions in Nine Strains of Borrelia burgdorferi

The availability of the amino acid sequenced for OspA from a number of different isolates, combined with peptide mapping and Western blot analysis, permitted the identification of the antigenic domains recognized by monoclonal antibodies (MAbs) and allowed inference of the key amino acid residues responsible for specific antibody reactivity.

Strains of Borrelia burgdorferi

Nine strains of *Borrelia*, including seven European strains and two North American strains, were used in this study of antibody binding domains of several proteins. Information concerning the strains is summarized in Table I, below.

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Table I. Representative Borrelia Strains

Strain	Location and Source	Reference for Strain	
K48	Czechoslovakia, Ixodes ricinus	none	
PGau	Germany, human ACA	Wilske, B. et al., <u>J. Clin.</u> <u>Microbiol. 32</u> :340-350 (1993)	
DK29	Denmark, human EM	Wilske, B. et al.	
PKo	Germany, human EM	Wilske, B. et al.	
PTrob	Germany, human skin	Wilske, B. et al.	
Ip3	Khabarovsk, Russia, I. persulcatus	Asbrink, E. <i>et al</i> ., <u>Acta</u> <u>Derm. Venereol. 64</u> : 506-512 (1984)	
Ip90	Khabarovsk, Russia, I. persulcatus	Asbrink, E. et al.	
25015	Millbrook, NY, I. persulcatus	Barbour, A.G. et al., <u>Curr.</u> <u>Microbiol. 8</u> :123-126 (1983)	
B31	Shelter Island, NY, I. scapularis	Luft, B.J. et al., <u>Infect.</u> <u>Immun. 60</u> : 4309-4321 (1992); ATCC 35210	
PKa1	Germany, human CSF	Wilske, B. et al.	
ZS7	Freiburg, Germany, I. ricinus	Wallich, R. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 8864 (1989)	
N40	Westchester Co., NY	Fikrig, E. et al., <u>Science</u> <u>250</u> :553-556 (1990)	
PHei	Germany, human CSF	Wilske, B. et al.	
ACAI	Sweden, human ACA	Luft, B. J. et al., <u>FEMS</u> <u>Microbiol. Lett. 93</u> :73-68 (1992)	
PBo	Germany, human CSF	Wilske, B. et al.	

ACA = patient with acrodermatitis chronica atrophicans; EM = patient with erythema migrans; CSF = cerebrospinal fluid of patient with Lyme disease

Strains K48, PGau and DK29 were supplied by R. Johnson, University of Minnesota; PKo and pTrob were provided by B. Wilske and V. Preac-Mursic of the

Pettenkhofer Institute, Munich, Germany; and Ip3 and Ip90 were supplied by L. Mayer of the Center for Disease Control, Atlanta, Georgia. The North American strains included strain 25015, provided by J. Anderson of the Connecticut Department of Agriculture; and strain B31 (ATCC 35210).

### Monoclonal Antibodies

Seven monoclonal antibodies (MAbs) were utilized in this study. Five of the MAbs (12, 13, 15, 83 and 336) were produced from hybridomas cloned and subcloned as previously 10 described (Schubach, W.H., et al., Infect. Immun. 59(6):1911-1915 (1991)). MAb H5332 (Barbour, A.G. et al., Infect. Immun. 41:795-804 (1983)) was a gift from Drs. Alan Barbour, University of Texas, and MAb CIII.78 (Sears, J.E. et al., J. Immunol. 147(6):1995-2000 (1991)) was a gift 15 from Richard A. Flavell, Yale University. MAbs 12 and 15 were raised against whole sonicated B3; MAb 336 was produced against whole PGau; and MAbs 13 and 83 were raised to a truncated form of OspA cloned from the K48 strain and expressed in E. coli using the T7 RNA polymerase system 20 (McGrath, B.C. et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York, pp. 365-370 (1993)). All MAbs were typed as being Immunoglobulin G (IgG).

Methods of Protein Cleavage, Western Blotting, and Amino-Terminal Sequencing

Prediction of the various cleavage sites was achieved by knowledge of the primary amino acid sequence derived from the full nucleotide sequences of OspA, many of which are currently available (see Table II, below). Cleavage sites can also be predicted based on the peptide sequence of OspA, which can be determined by standard techniques after isolation and purification of OspA by the method described above. Cleavage of several OspA isolates was

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conducted to determine the localization of monoclonal antibody binding of the proteins.

Hydroxylamine-HCl (HA), N-chlorosuccinimide (NCS), and cyanogen bromide cleavage of OspA followed the methods

5 described by Bornstein (Biochem. 9 (12):2408-2421 (1970)), Shechter et al., (Biochem. 15 (23):5071-5075 (1976)), and Gross (in Hirs, C.H.W. (ed): Methods in Enzymology, (N.Y. Acad. Press), 11:238-255 (1967)) respectively. Protease cleavage by endoproteinase, Asp-N (Boehringer Mannheim,

10 Indianapolis, Indiana), was performed as described by Cleveland D.W. et al., (J. Biol. Chem. 252:1102-1106 (1977)). Ten micrograms of OspA were used for each reaction. The ratio of enzyme to OspA was approximately 1 to 10 (w/w).

- Proteins and peptides generated by cleavage were separated by SDS-polyacrylamide gel electrophoresis (SDS-PAGE) (Laemmli, U.K., Nature (London) 227:680-685 (1970)), and electroblotted onto immobilon Polyvinylidine Difluoride (PVDF) membranes (Ploskal, M.G. et al., Biotechniques
- 20 4:272-283 (1986)). They were detected by amido black staining or by immunostaining with murine MAbs, followed by alkaline phosphatase-conjugated goat antimouse IgG. Specific binding was detected using a 5-bromo-4-chloro-3indolylphosphate (BCIP)/nitroblue tetrazolium (NBT)
- 25 developer system (KPL Inc., Gathersburg, Maryland).

  In addition, amino-terminal amino acid sequence
  analysis was carried out on several cleavage products, as
  described by Luft et al. (Infect. Immun. 57:3637-3645
  (1989)). Amido black stained bands were excised from PVDF
- 30 blots and sequenced by Edman degradation using a Biosystems model 475A sequenator with model 120A PTH analyzer and model 900A control/data analyzer.

Cleavage Products of Outer Surface Protein A Isolates Purified OspA-B31, labeled with 14C-palmitic acid, was fragmented with hydroxylamine-HCl (HA) into two peptides, designated HA1 and HA2 (data not shown). The HA1 band migrated at 27 KD and retained its radioactivity, indicating that the peptide included the lipidation site at the N-terminus of the molecule (data not shown). From the predicted cleavage point, HA1 should correspond to residues 1 to 251 of OspA-B31. HA2 had a MW of 21.6 KD by SDS-PAGE, 10 with amino-terminal sequence analysis showing it to begin at Gly72, i.e. residues 72 to 273 of OspA-B31. By contrast, HA cleaved OspA-K48 into three peptides, designated HA1, HA2, and HA3 with apparent MWs of 22KD, 16 KD and 12 KD, respectively. Amino-terminal sequencing 15 showed HA1 to start at Gly72, and HA3 at Gly142. found to have a blocked amino-terminus, as was observed for the full-length OspA protein. HA1, 2 and 3 of OspA-K48 were predicted to be residues 72-274, 1 to 141 and 142 to 274, respectively.

N-Chlorosuccinimide (NCS) cleaves tryptophan (W), which is at residue 216 of OspA-B31 or residue 217 of OspA-K48 (data not shown). NCS cleaved OspA-B31 into 2 fragments, NCS1, with MW of 23 KD, residues 1-216 of the protein, and NCS2 with a MW of 6.2 KD, residues 217 to 273 (data not shown). Similarly, K48 OspA was divided into 2 pieces, NCS1 residues 1-217, and NCS2 residues 218 to 274 (data not shown).

Cleavage of OspA by cyanogen bromide (CNBr) occurs at the carboxy side of methionine, residue 39. The major fragment, CNBrl, has a MW of 25.7 KD, residues 39-274 by amino-terminal amino acid sequence analysis (data not shown). CNBr2 (about 4 KD) could not be visualized by amido black staining; instead, lightly stained bands of about 20 KD MW were seen. These bands reacted with anti-

OspA MAbs, and most likely were degradation products due to cleavage by formic acid.

Determination of Antibody Binding Domains for Anti-OspA Monoclonal Antibodies

The cleavage products of OspA-B31 and OspA-K48 were analyzed by Western blot to assess their ability to bind to the six different MAbs. Preliminary Western blot analysis of the cleavage products demonstrated that strains K48 and DK29 have similar patterns of reactivity, as do IP3, PGau

and PKo. The OspA of strain PTrob was immunologically distinct from the others, being recognized only by MAb 336. MAb 12 recognized only the two North American strains, B31 and 25015. When the isolates were separated into genogroups, it was remarkable that all the MAbs, except MAb 12, crossed over to react with multiple genogroups.

MAb12, specific for OspA-B31, bound to both HA1 and HA2 of OspA-B31. However, cleavage of OspA-B31 by NCS at residue Trp216 created fragments which did not react with MAb12, suggesting that the relevant domain is near or is structurally dependent upon the integrity of this residue (data not shown). MAb 13 bound only to OspA-K48, and to peptides containing the amino-terminus of that molecule (e.g. HA2; NCS1). It did not bind to CNBr1 residues 39 to 274. Thus the domain recognized by MAb13 is in the amino-terminal end of OspA-K48, near Met38.

MAbl5 reacts with the OspA of both the B31 and K48 strains, and to peptides containing the N-terminus of OspA, such as HA1 of OspA-B31 and NCS1, but not to peptides HA2 of OspA-B31 and HA1 of OspA-K48 (data not shown). Both peptides include residue 72 to the C-terminus of the molecules. MAbl5 bound to CNBr1 of OspA-K48, indicating the domain for this antibody to be residues 39 to 72, specifically near Gly72 (data not shown).

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MAD83 binds to OspA-K48, and to peptides containing the C-terminal portion of the molecule, such as HA1. They do not bind to HA2 of OspA-K48, most likely because the C-terminus of HA2 of OspA-K48 ends at 141. Similar to MAb12 and OspA-B31, binding of MAbs 83 and CIII.78 is eliminated by cleavage of OspA at the tryptophan residue. Thus binding of MAbs 12, 83 and CIII.78 to OspA depends on the structural integrity of the Trp216 residue, which appears to be critical for antigenicity. Also apparent is that, although these MAbs bind to a common antigenic domain, the precise epitopes which they recognize are distinct from one another given the varying degrees of cross-reactivity to these MAbs among strains.

Although there is similar loss of binding activity of 15 MAb336 with cleavage at Trp216, this MAb does not bind to HA1 of OspA-B31, suggesting the domain for this antibody includes the carboxy-terminal end of the molecule, inclusive of residues 251 to 273. Low MW peptides, such as HA3 (10 KD) and NCS2 (6KD), of OspA-K48 do not bind this MAb on Western blots. In order to confirm this 20 observation, we tested binding of the 6 MAbs with a recombinant fusion construct p3A/EC that contains a trpE leader protein fused with residues 217 to 273 of OspA-B31 (Schubach, W.H. et al., <u>Infect. Immun. 59(6)</u>: 1911-1915 (1991)). Only MAb336 reacted with this construct (data not 25 shown). Peptides and antigenic domains localized by fragmentation of OspA are summarized in Figure 1.

Mapping of Domains to Define the Molecular Basis for the Serotype Analysis

To define the molecular basis for the serotype analysis of OspA, we compared the derived amino acid sequences of OspA for the nine isolates (Figure 2). At the amino terminus of the protein, these predictions can be more precise given the relatively small number of amino

acid substitutions in this region compared to the carboxy terminus. Domain 1, which is recognized by MAb13, includes residues Leu34 to Leu41. MAb13 only binds to the OspA of species K48, DK29 and IP90. Within this region, residue 37 5 is variable, however Gly37 is conserved amongst the three reactive strains. When Gly37 is changed to Glu37, as it is in OspA of strains B31, pTrob, PGau, and PKo, MAb13 does not recognize the protein (data not shown). By similar analysis, it can be seen that Asp70 is a crucial residue 10 for Domain 2, which includes residues 65 to 75 and is recognized by MAb15. Domain 3 is reactive with MAbs H5332, 12 and 83, and includes residues 190-220. It is clear that significant heterogeneity exists between MAbs reactive with this domain, and that more than one conformational epitope 15 must be contained within the sequence. Domain 4 binds MAb336, and includes residues 250 to 270. In this region, residue 266 is variable and therefore may be an important determinant. It is apparent, however, that other determinants of the reactivity of this monoclonal antibody 20 reside in the region comprising amino acids 217-250. Furthermore, the structural integrity of Trp216 is essential for antibody reactivity in the intact protein. Finally, it is important to stress that Figure 2 indicates only the locations of the domains, and does not necessarily 25 encompass the entire domain. Exact epitopes are being analyzed by site-directed mutagenesis of specific residues.

Overall, evidence suggests that the N-terminal portion is not the immunodominant domain of OspA, possibly by virtue of its lipidation, and the putative function of the lipid moiety in anchoring the protein to the outer envelope. The C-terminal end is immunodominant and includes domains that account in part for structural heterogeneity (Wilske, B. et al., Med. Microbiol. Immunol. 181: 191-207 (1992)), and may provide epitopes for antibody

neutralization (Sears, J.E. et al., J. Immunol. 147(6):
1995-2000 (1991)), and relate to other activities, such as
the induction of T-cell proliferation (Shanafel, M.M., et
al., J. Immunol. 148: 218-224 (1992)). There are common
epitopes in the carboxy-end of the protein that are shared
among genospecies which may have immunoprotective potential
(Wilske, B., et al., Med. Microbiol. Immunol. 181: 191-207
(1992)).

Prediction of secondary structure on the basis of
hydropathy analysis and circular dichroism and fluorescence
spectroscopy measurements (McGrath, B.C., et al., Vaccines,
Cold Spring Harbor Laboratory Press, Plainview, New York;
pp. 365-370 (1993)) suggest domains 3 and 4 to be in a
region of the molecule with a propensity to form alphahelix, whereas domains 1 and 2 occur in regions predicted
to be beta-sheets (see Figure 1). These differences may
distinguish domains in accessibility to antibody or to
reactive T-cells (Shanafel, M.M. et al., J. Immunol. 148:
218-224 (1992)). Site-directed mutagenesis of specific
epitopes, as described below in Example 2, aids in
identifying exact epitopes.

## Example 2. Identification of an Immunologically Important Hypervariable Domain of the Major Outer Surface Protein A of Borrelia

This Example describes epitope mapping studies using chemically cleaved OspA and TrpE-OspA fusion proteins. The studies indicate a hypervariable region surrounding the single conserved tryptophan residue of OspA (at residue 216, or in some cases 217), as determined by a moving window population analysis of OspA from fifteen European and North American isolates of Borrelia. The hypervariable region is important for immune recognition.

Site-directed mutagenesis was also conducted to examine the hypervariable regions more closely. Fluorescence and circular dichroism spectroscopy have indicated that the conserved tryptophan is part of an 5 alpha-helical region in which the tryptophan is buried in a hydrophobic environment (McGrath, B.C., et al., Vaccines, Cold Spring Harbor Laboratory Press, Plainview, New York; pp. 365-370 (1993)). More polar amino acid side-chains flanking the tryptophan are likely to be exposed to the 10 hydrophilic solvent. The hypervariability of these solvent-exposed residues among the various strains of Borrelia suggested that these amino acid residues may contribute to the antigenic variation in OspA. Therefore, site-directed mutagenesis was performed to replace some of 15 Tthe potentially exposed amino acid side chains in the protein from one strain with the analogous residues of a second strain. The altered proteins were then analyzed by Western Blot using monoclonal antibodies which bind OspA on the surface of the intact, non-mutated spirochete. 20 results indicated that certain specific amino acid changes near the tryptophan can abolish reactivity of OspA to these monoclonal antibodies.

### A. Verification of Clustered Polymorphisms in Outer Surface Protein A Sequences

Cloning and sequencing of the OspA protein from fifteen European and North American isolates (described above in Table I) demonstrated that amino acid polymorphism is not randomly distributed throughout the protein; rather, polymorphism tended to be clustered in three regions of OspA. The analysis was carried out by plotting the moving, weighted average polymorphism of a window (a fixed length subsection of the total sequence) as it is slid along the sequence. The window size in this analysis was thirteen amino acids, based upon the determination of the largest

number of significantly deviating points as established by the method of Tajima (<u>J. Mol. Evol. 33</u>: 470-473 (1991)). The average weighted polymorphism was calculated by summing the number of variant alleles for each site. Polymorphism calculations were weighted by the severity of amino acid replacement (Dayhoff, M.O. et al., in: Dayhoff, M.O. (ed.) Atlas of Protein Sequence and Structure NBRF, Washington, Vol. 5, Suppl. 3: 345 (1978)). The sum was normalized by the window size and plotted. The amino acid sequence 10 position corresponds to a window that encompasses amino acids 1 through 13. Bootstrap resampling was used to generate 95% confidence intervals on the sliding window analysis. Since Borrelia has been shown to be clonal, the bootstrap analysis should give a reliable estimate of the 15 expected variance out of polymorphism calculations. bootstrap was iterated five hundred times at each position, and the mean was calculated from the sum of all positions. The clonal nature of Borrelia ensures that the stochastic variance that results from differing genealogical histories of the sequence positions (as would be expected if 20 recombination were prevalent) will be minimized.

This test verified that the three regions around the observed peaks all have significant excesses of polymorphism. Excesses of polymorphism were observed in the regions including amino acid residues 132-145, residues 163-177, and residues 208-221 (Figure 3). An amino acid alignment between residues 200 and 220 for B31, K48 and the four site-directed mutants is shown in Figure 4. The amino acid 208-221 region includes the region of OspA which has been modeled as an oriented alpha-helix in which the single tryptophan residue at amino acid 216 is buried in a hydrophobic pocket, thereby exposing more polar amino acids to the solvent (Figure 5) (France, L.L., et al., Biochem. Biophys. Acta 1120: 59 (1992)). These potentially solvent-exposed residues showed considerable variability among the

OspAs from various strains and may be an important component of OspA antigenic variation. For the purposes of generating chimeric proteins, the hypervariable domains of interest are <u>Domain A</u>, which includes amino acid residues 120-140 of OspA; <u>Domain B</u>, which includes residues 150-180; and <u>Domain C</u>, which includes residues 200-216 or 217.

- B. Site-Directed Mutagenesis of the Hypervariable Region
  Site-directed mutagenesis was performed to convert
  residues within the 204-219 domain of the recombinant B31

  10 OspA to the analogous residues of a European OspA variant,
  K48. In the region of OspA between residues 204 and 219,
  which includes the helical domain (amino acids 204-217),
  there are seven amino acid differences between OspA-B31 and
  OspA-K48. Three oligonucleotides were generated, each
  containing nucleotide changes which would incorporate K48
  amino acids at their analogous positions in the B31 OspA
  protein. The oligos used to create the site-directed
  mutants were:
- 5'-CTTAATGACTCTGACACTAGTGC-3' (#613, which converts

  20 threonine at position 204 to serine, and serine at 206 to
  threonine (Thr204-Ser, Thr206-Ser)) (SEQ ID NO. 1);

  5'-GCTACTAAAAAAACCGGGAAATGGAATTCA-3' (#625, which converts
  alanine at 214 to glycine, and alanine at 215 to lysine
  (Ala214-Gly, Ala215-Lys)) (SEQ ID NO. 2); and

  25 5'-GCAGCTTGGGATTCAAAAACATCCACTTTAACA-3' (#640, which
  converts asparagine at 217 to aspartate, and glycine at
  219 to lysine (Asn217-Asp, Gly219-Lys)) (SEQ ID NO. 3).

Site-directed mutagenesis was carried out by performing mutagenesis with pairs of the above oligos.

Three site-directed mutants were created, each with two changes: OspA 613 (Thr204-Ser, Thr206-Ser), OspA 625 (Ala214-Gly, Ala215-Lys), and 640 (Asn217-Asp, Gly219-Lys). There were also two proteins with four changes: OspA 613/625 (Thr204-Ser, Thr206-Ser, Ala214-Gly, Ala215-Lys)

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and OspA 613/640 (Thr204-Ser, Thr206-Ser, Asn217-Asp, Gly219-Lys).

Specificity of Antibody Binding to Epitopes of the Non-mutated Hypervariable Region

Monoclonal antibodies that agglutinate spirochetes, including several which are neutralizing in vitro, recognize epitopes that map to the hypervariable region around Trp216 (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983); Schubach, W.H. et al., Infect. and Immun. 59:

10 1911 (1991)). Western Blot analysis demonstrated that chemical cleavage of OspA from the B31 strain at Trp 216 abolishes reactivity of the protein with the agglutinating Mab 105, a monoclonal raised against B31 spirochetes (data not shown). The reagent, n-chlorosuccinimide (NCS),

15 cleaves OspA at the Trp 216, forming a 23.2kd fragment and a 6.2kd peptide which is not retained on the Imobilon-P membrane after transfer. The uncleaved material binds Mab 105; however, the 23.2kd fragment is unreactive. Similar Western blots with a TrpE-OspA fusion protein containing

20 the carboxy-terminal portion of the OspA protein demonstrated that the small 6.2kd piece also fails to bind Mab 105 (Schubach, W.H. et al., <u>Infect. and Immun. 59</u>: 1911 (1991)).

Monoclonal antibodies H5332 and H3TS (Barbour, A.G. et al., Infect. and Immun. 41: 759 (1983)) have been shown by immunofluorescence to decorate the surface of fixed spirochetes (Wilske, B. et al., World J. Microbiol. 7: 130 (1991)). These monoclonals also inhibit the growth of the organism in culture. Epitope mapping with fusion proteins has confirmed that the epitopes which bind these Mabs are conformationally determined and reside in the carboxy half of the protein. Mab H5332 is cross-reactive among all of the known phylogenetic groups, whereas Mab H3TS and Mab 105 seem to be specific to the B31 strain to which they were

raised. Like Mab 105, the reactivities of H5332 and H3TS to OspA are abrogated by fragmentation of the protein at Trp216 (data not shown). Mab 336 was raised to whole spirochetes of the strain P/Gau. It cross-reacts to OspA from group 1 (the group to which B31 belongs) but not to group 2 (of which K48 is a member). Previous studies using fusion proteins and chemical cleavage have indicated that this antibody recognizes a domain of OspA in the region between residues 217 and 273 (data not shown). All of these Mabs will agglutinate the B31 spirochete.

Western Blot Analysis of Antibody Binding to Mutated Hypervariable Regions

Mabs were used for Western Blot analysis of the sitedirected OspA mutants induced in E. coli using the T7 15 expression system (Dunn, J.J. et al., Protein Expression and Purification 1: 159 (1990)). E. coli cells carrying Pet9c plasmids having a site-directed OspA mutant insert were induced at mid-log phase growth with IPTG for four hours at 37°C. Cell lysates were made by boiling an aliquot of the induced cultures in SDS gell loading dye, and this material was then loaded onto a 12% SDS gell (BioRad mini-Protean II), and electrophoresed. proteins were then transferred to Imobilon-P membranes (Millipore) 70V, 2 hour at 4°C using the BioRad mini 25 transfer system. Western analysis was carried out as described by Schubach et al. (Infect. Immun. 59: 1911 (1991)).

Western Blot analysis indicated that only the 625 mutant (Ala214-Gly and Ala215-Lys) retained binding to the agglutinating monoclonal H3TS (data not shown). However, the 613/625 mutant which has additional alterations to the amino terminus of Trp216 (Ser204-Thr and Thr206-Ser) did not bind this monoclonal. Both 640 and 613/640 OspAs which have the Asn217-Asp and Gly219-Lys changes on the carboxy-

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terminal side of Trp216 also failed to bind Mab H3TS. This indicated that the epitope of the B31 OspA which binds H3TS is comprised of amino acid side-chains on both sides of Trp216.

The 613/625 mutant failed to bind Mabs 105 and H5332, while the other mutants retained their ability to bind these Mabs. This is important in light of the data using fusion proteins that indicate that Mab 105 behaves more like Mab H3TS in terms of its serotype specificity and binding to OspA (Wilske, B. et al., Med. Microbiol.

Immunol. 181: 191 (1992)). The 613/625 protein has, in addition to the differences at residues Thr204 and Ser206, changes immediately amino-terminal to Trp216 (Ala214-Gly and Ala215-Lys). The abrogation of reactivity of Mabs 105 and H5332 to this protein indicated that the epitopes of OspA which bind these monoclonals are comprised of residues on the amino-terminal side of Trp216.

The two proteins carrying the Asn217-Asp and Gly219-Lys replacements on the carboxy-terminal side of Trp216 (OspAs 640 and 613/640) retained binding to Mabs 105 and H5332; however, they failed to react with Mab 336, a monoclonal which has been mapped with TrpE-OspA fusion proteins and by chemical cleavage to a more carboxy-terminal domain. This result may explain why Mab 336 failed to recognize the K48-type of OspA (Group 2).

It is clear that amino acids Ser204 and Thr206 play an important part in the agglutinating epitopes in the region of the B31 OspA flanking Trp216. Replacement of these two residues altered the epitopes of OspA that bind Mabs 105, 30 H3TS and H5332. The ability of the 640 changes alone to abolish reactivity of Mab 336 indicated that Thr204 and Ser206 are not involved in direct interaction with Mab 336.

The results indicated that the epitopes of OspA which are available to Mabs that agglutinate spirochetes are comprised at least in part by amino acids in the immediate

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vicinity of Trp216. Since recent circular dichroism analysis indicated that the structures of B31 and K48 OspA differ very little within this domain, it is unlikely that the changes made by mutation have radically altered the overall structure of the OspA protein (France, L.L. et al., Biochem. Biophys. Acta 1120: 59 (1992); and France et al., Biochem. Biophys Acta, submitted (1993)). This hypothesis is supported by the finding that the recombinant, mutant OspAs exhibit the same high solubility and purification properties as the parent B31 protein (data not shown).

In summary, amino acid side-chains at Ser204 and Thr206 are important for many of the agglutinating epitopes. However, a limited set of conservative changes at these sites were not sufficient to abolish binding of all of the agglutinating Mabs. These results suggested that the agglutinating epitopes of OspA are distinct, yet may have some overlap. The results also supported the hypothesis that the surface-exposed epitope around Trp216 which is thought to be important for immune recognition and neutralization is a conformationally-determined and complex domain of OspA.

### EXAMPLE 3. Borrelia Strains and Proteins

Proteins and genes from any strain of Borrelia can be utilized in the current invention. Representative strains are summarized in Table I, above.

### A. Genes Encoding Borrelia Proteins

The chimeric peptides of the current invention can comprise peptides derived from any Borrelia proteins.

Representative proteins include OspA, OspB, OspC, OspD,

pl2, p39, p41 (fla), p66, and p93. Nucleic acid sequences encoding several Borrelia proteins are presently available (see Table II, below); alternatively, nucleic acid

sequences encoding Borrelia proteins can be isolated and characterized using methods such as those described below.

Table II. References for Nucleic Acid Sequences for Several Proteins of Various Borrelia Strains

Strai n	p93	OspA	p41 (fla)
K48	X69602 (SID 67)	X62624 (SID 8)	X69610 (SID 49)
PGau	SID 73	X62387 (SID 10)	X69612 (SID 51)
DK29 ·	_	X63412 (SID 137)	X69608 (SID 53)
PKo	X69803 (SID 77)	X65599 (SID 141)	X69613 (SID 131)
PTrob	X69604 (SID 71)	X65598 (SID 135)	X69614 (SID 55)
Ip3	-	X70365 (SID 140)	-
Ip90	ND	Kryuchechnikov, V.N. et al., J.Microbiol. Epid. Immunobiol. 12:41-44 (1988) (SID 138)	<b>-</b> .
25015	X70365 (SID 75)	Fikrig, E.S. et al., <u>J. Immunol. 7</u> :2256- 2260 1992) SID 12)	-
B31	Perng, G.C. et al., <u>Infect.</u> <u>Immun. 59:</u> 2070- 74 (1992); Luft, B.J. et al., <u>Infect.</u> <u>Immun: 60:</u> 4309- 4321 (1992) (SID 65)	Bergstrom, S. et al., <u>Mol. Microbiol.</u> 3:479-486 (1989) (SID 6)	Gassmann, G.S. et al., <u>Nucl.</u> <u>Acids Res. 17</u> : 3590 (1989) (SID 127)
PKa1	-	X69606 (SID 132)	X69611 (SID 129)
257	-	Jonsson, M. et al., <u>Infect. Immun.</u> <u>60</u> :1845-1853 (1992) (SID 134)	-
N40	-	Kryuchechnikov, V.N. et al. (SID 133)	-
PHei	-	X65600 (SID 136)	-
ACAI	-	Kryuchechnikov, V.N. et al. (SID 142)	-
PBo	X69601 (SID 69)	X65605 (SID 139)	X69610 (SID 130)

Numbers with an "X" prefix are GenBank data base accession numbers. SID = SEQ ID NO.

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### B. Isolation of Borrelia Genes

Nucleic acid sequences encoding full length, lipidated proteins from known Borrelia strains were isolated using the polymerase chain reaction (PCR) as described below. In addition, nucleic acid sequences were generated which encoded truncated proteins (proteins in which the lipidation signal has been removed, such as by eliminating the nucleic acid sequence encoding the first 18 amino acids, resulting in non-lipidated proteins). proteins were generated which encoded polypeptides of a particular gene (i.e., encoding a segment of the protein which has a different number of amino acids than the protein does in nature). Using similar methods as those described below, primers can be generated from known 15 enucleic acid sequences encoding Borrelia proteins and used to isolate other genes encoding Borrelia proteins. can be designed to amplify all of a gene, as well as to amplify a nucleic acid sequence encoding truncated protein sequences, such as described below for OspC, or nucleic 20 acid sequences encoding a polypeptide derived from a Borrelia protein. Primers can also be designed to incorporate unique restriction enzyme cleavage sites into the amplified nucleic acid sequences. Sequence analysis of the amplified nucleic acid sequences can then be performed 25 using standard techniques.

> Cloning and Sequencing of OspA Genes and Relevant Nucleic Acid Sequences

Borrelia OspA sequences were isolated in the following manner: 100  $\mu$ l reaction mixtures containing 50 mM KCl, 10 mM TRIS-HCl (pH 8,3), 1.5 mM MgCl<sub>2</sub>, 200  $\mu$ M each NTP, 2.5 units of TaqI DNA polymerase (Amplitaq, Perkin-Elmer/Cetus) and 100 pmol each of the 5' and 3' primers (described below) were used. Amplification was performed in a Perkin-Elmer/Cetus thermal cycler as described (Schubach, W.H. et

al., Infect. Immun. 59:1811-1915 (1991)). The amplicon was visualized on an agarose gel by ethidium bromide staining. Twenty nanograms of the chloroform-extracted PCR product were cloned directly into the PC-TA vector (Invitrogen) by following the manufacturer's instructions. Recombinant colonies containing the amplified fragment were selected, the plasmids were prepared, and the nucleic acid sequence of each OspA was determined by the dideoxy chaintermination technique using the Sequenase kit (United States Biochemical). Directed sequencing was performed with M13 primers followed by OspA-specific primers derived from sequences, previously obtained with M13 primers.

Because the 5' and 3' ends of the OspA gene are highly conserved (Fikrig, E.S. et al., J. Immunol. 7:2256-2260

15 (1992); Bergstrom, S. et al., Mol. Microbiol. 3: 479-486 (1989); Zumstein, G. et al., Med. Microbiol. Immunol. 181: 57-70 (1992)), the 5' and 3' primers for cloning can be based upon any known OspA sequences. For example, the following primers based upon the OspA nucleic acid sequence 20 from strain B31 were used:

5'-GGAGAATATTATGAAA-3' (-12 to +6) (SEQ ID NO. 4); and 5'-CTCCTTATTTTAAAGCG-3' (+826 to +809) (SEQ ID NO. 5). (Schubach, W.H. et al., <u>Infect. Immun 59</u>:1811-1915 (1991)).

OspA genes isolated in this manner include those for strains B31, K48, PGau, and 25015; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 6 (OspA-B31), SEQ ID NO. 8 (OspA-K48), SEQ ID NO. 10 (OspA-PGau), and SEQ ID NO. 12 (OspA-25015). An alignment of these and other OspA nucleic acid sequences is shown in Figure 42. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 7 (OspA-B31), SEQ ID NO. 9 (OspA-K48), SEQ ID NO. 11 (OspA-PGau), and SEQ ID NO. 13 (OspA-25015).

The following primers were used to generate specific nucleic acid sequences of the OspA gene, to be used to

generate chimeric nucleic acid sequences (as described in Example 4):

- 5'-GTCTGCAAAACCATGACAAG-3' (plus strand primer #369) (SEQ ID NO. 14);
- 5 5'-GTCATCAACAGAAGAAAATTC-3' (plus strand primer #357) (SEO ID NO 15);
  - 5'-CCGGATCCATATGAAAAAATATTTATTGGG-3' (plus strand primer #607) (SEQ ID NO. 16);
- 5'-CCGGGATCCATATGGCTAAGCAAAATGTTAGC-3' (plus strand primer 10 #584) (SEQ ID NO. 17);
  - 5'-GCGTTCAAGTACTCCAGA-3' (minus strand primer #200) (SEQ ID NO. 18);
    - 5'-GATATCTAGATCTTATTTTAAAGCGTT-3' (minus strand primer #586) (SEQ ID NO. 19); and
- 15 5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAT-3' (minus strand primer #1169) (SEQ ID NO. 20).

#### Cloning and Sequencing of OspB

Similar methods were also used to isolate OspB genes.
One OspB genes isolated is represented as SEQ ID NO. 21
20 (OspB-B31); its encoded amino acid sequence is SEQ ID NO.
22.

The following primers were used to generate specific nucleic acid sequences of the OspB gene, to be used in generation of chimeric nucleic acid sequences (see Example 25 4):

- 5'-GGTACAATTACAGTACAA-3' (plus strand primer #721) (SEQ ID NO. 23);
- 5'-CCGAGAATCTCATATGGCACAAAAAGGTGCTGAGTCAATTGG-3' (plus strand primer #1105) (SEQ ID NO. 24);
- 5'-CCGATATCGGATCCTATTTTAAAGCGTTTTTAAGC-3' (minus strand
  primer # 1106) (SEQ ID NO. 25); and
  5'-GGATCCGGTGACCTTTTAAAGCGTTTTTAAG-3' (minus strand primer
  #1170) (SEQ ID NO. 26).

Cloning and Sequencing of OspC

Similar methods were also used to isolate OspC genes. The following primers were used to isolate entire OspC genes from Borrelia strains B31, K48, PKO, and pTrob: 5'-GTGCGCGACCATATGAAAAAGAATACATTAAGTGCG-3' (plus strand primer having Ndel site combined with start codon) (SEQ ID NO. 27), and

5'-GTCGGCGGATCCTTAAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer having BamH1 site followed by stop codon) (SEQ ID NO. 28).

The nucleic acid sequences of the OspC genes were then determined by the dideoxy chain-termination technique using the Sequenase kit (United States Biochemical). OspC genes isolated and sequenced in this manner include those for strains B31, K48, PKo, and Tro; the nucleic acid sequences are depicted in the sequence listing as SEQ ID NO. 29 (OspC-B31), SEQ ID NO. 31 (OspC-K48), SEQ ID NO. 33 (OspC-PKo), and SEQ ID NO. 35 (OspC-Tro). An alignment of these sequences is shown in Figure 38. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 30 (OspC-B31), SEQ ID NO. 32 (OspC-K48), SEQ ID NO. 34 (OspC-PKo), and SEQ ID NO. 36 (OspC-Tro).

Truncated OspC genes were generated using other

25 primers. These primers were designed to amplify nucleic

acid sequences, derived from the OspC gene, that lacked the nucleic acids encoding the signal peptidase sequence of the full-length protein. The primers corresponded to bp 58-75 of the natural protein, with a codon for Met-Ala attached

30 ahead. For strain B31, the following primer was used:

5'-GTGCGCGACCATATGGCTAATAATTCAGGGAAAGAT-3' (SEQ ID NO.

37).

For strain PKo,

5'-GTGCGCGACCATATGGCTAGTAATTCAGGGAAAGGT-3' (SEQ ID NO. 38)

For strains pTrob and K48, 5'-GTGCGCGACCATATGGCTAATAATTCAGGTGGGGAT-3' (SEQ ID NO. 39) was used.

Additional primers were also designed to amplify nucleic acids encoding particular polypeptides, for use in creation of chimeric nucleic acid sequences (see Example 4). These primers included:

- 5'-CTTGGAAAATTATTTGAA-3' (plus strand primer #520) (SEQ ID NO. 40);
- 5'-CACGGTCACCCCATGGGAAATAATTCAGGGAAAGG-3' (plus strand primer #58) (SEQ ID NO. 41);
  - 5'-TATAGATGACAGCAACGC-3' (minus strand primer #207) (SEQ ID NO. 42); and
- 5'-CCGGTGACCCCATGGTACCAGGTTTTTTTGGACTTTCTGC-3' (minus strand primer #636) (SEQ ID NO. 43).

Cloning and Sequencing of OspD

Similar methods can be used to isolate OspD genes. An alignment of four OspD nucleic acid sequences (from strains pBo, PGau, DK29, and K48) is shown in Figure 39.

20 Cloning and Sequencing of p12

The p12 gene was similarly identified. Primers used to clone the entire p12 gene included: 5'CCGGATCCATATGGTTAAAAAAATAATATTTATTTC-3' (forward primer # 757) (SEQ ID NO. 44); and 5'-

25 GATATCTAGATCTTTAATTGCTCTGCTCACTCTCTC-3' (reverse primer #758) (SEQ ID NO. 45).

To amplify a truncated p12 gene (one in which the transcribed protein is non-lipidated, and begins at amino acid 18 of the native sequence), the following primers were used: 5'-CCGGGATCCATATGGCTAGTGCAATTGGTCGTGG-3' (forward primer # 759) (SEQ ID NO. 46); and primer #758 (SEQ ID NO. 45).

# Cloning and Sequencing of p41 (fla)

A similar approach was used to clone and sequence genes encoding the p41 (fla) protein. The p41 sequences listed in Table II with GenBank accession numbers were isolated using the following primers from strain B31: 5'-ATGATTATCAATCATAAT-3' (+1 to +18) (SEQ ID NO. 47); and 5'-TCTGAACAATGACAAAAC-3' (+1008 to +991) (SEQ ID NO. 48). The nucleic acid sequences of p41 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 51 (p41-PGau), and SEQ ID NO. 53 (p41-DK29). An alignment of 10 several p41 nucleic acid sequences, including those for strains B31, pKa1, PGau, pBo, DK29, and pKo, is shown in Figure 41. The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 50 (p41-K48), SEQ ID NO. 52 (p41-PGau), SEQ ID NO. 54 (p41-DK29), SEQ ID NO. 56 (p41-PTrob), and SEQ ID NO. 58 (p41-PHei).

Other primers were designed to amplify nucleic acid sequences encoding polypeptides of p41, to be used in chimeric nucleic acid sequences. These primers included: 5'-TTGGATCCGGTCACCCCATGGCTCAATATAACCAATG-3' (minus strand primer #122) (SEQ ID NO. 59);

5'-TTGGATCCGGTCACCCCATGGCTTCTCAAAATGTAAG-3' (plus strand primer # 140) (SEQ ID NO. 60);

5'-TTGGATCCGGTGACCAACTCCGCCTTGAGAAGG-3' (minus strand primer # 234) (SEQ ID NO. 61); and 5'-TTGGATCCGGTGACCTATTTGAGCATAAGATGC-3' (minus strand primer #141) (SEQ ID NO. 62).

#### Cloning and Sequencing of p93

The same approach was also used to clone and sequence p93 protein. Genes encoding p93, as listed in Table II with GenBank accession numbers, were isolated by this method with the following primers from strain B31:

- 5'-GGTGAATTTAGTTGGTAAGG-3' (-54 to -35) (SEQ ID NO. 63); and
- 5'-CACCAGTTTCTTTAAGCTGCTCCTGC-3' (+1117 to +1092) (SEQ ID NO. 64).
- The nucleic acid sequences of p93 isolated in this manner are depicted in the sequence listing as SEQ ID NO. 65 (p93-B31), SEQ ID NO. 67 (p93-K48) SEQ ID NO. 69 (p93-PBo), SEQ ID NO. 71 (p93-PTrob), SEQ ID NO. 73 (p93-PGau), SEQ ID NO. 75 (p93-25015), and SEQ ID NO. 77 (p93-PKo).
- The amino acid sequences of the proteins encoded by these nucleic acid sequences are represented as SEQ ID NO. 66 (p93-B31), SEQ ID NO. 68 (p93-K48) SEQ ID NO. 70 (p93-PBo), SEQ ID NO. 72 (p93-PTrob), SEQ ID NO. 74 (p93-PGau), SEQ ID NO. 76 (p93-25015), and SEQ ID NO. 78 (p93-PKo).
- Other primers were used to amplify nucleic acid sequences encoding polypeptides of p93 to be used in generating chimeric nucleic acid sequences. These primers included:
- 5'-CCGGTCACCCCATGGCTGCTTTAAAGTCTTTA-3' (plus strand primer 20 #475) (SEQ ID NO. 79);
  - 5'-CCGGTCACCCCATGAATCTTGATAAAGCTCAG-3' (plus strand primer #900) (SEQ ID NO. 80);
  - 5'-CCGGTCACCCCATGGATGAAAAGCTTTTAAAAAGT-3' (plus strand primer #1168) (SEQ ID NO. 81);
- 5'-CCGGTCACCCCATGGTTGAGAAATTAGATAAG-3' (plus strand primer #1423) (SEQ ID NO. 82); and
  - 5'-TTGGATCCGGTGACCCTTAACTTTTTTAAAG-3' (minus strand primer # 2100) (SEQ ID NO. 83).

## C. Expression of Proteins from Borrelia Genes

The nucleic acid sequences described above can be incorporated into expression plasmids, using standard techniques, and transfected into compatible host cells in order to express the proteins encoded by the nucleic acid

sequences. As an example, the expression the pl2 gene and the isolation of pl2 protein is set forth.

Amplification of the pl2 nucleic acid sequence was conducted with primers that included a NdeI restriction site into the nucleic acid sequence. The PCR product was extracted with phenol/chloroform and precipitated with The precipitated product was digested and ligated into an expression plasmid as follows:  $15 \mu l$ (approximately 1  $\mu$ g) of PCR DNA was combined with 2  $\mu$ l 10X. restriction buffer for NdeI (Gibco/BRL), 1  $\mu$ l NdeI 10 (Gibco/BRL), and 2  $\mu$ l distilled water, and incubated overnight at 37°C. This mixture was subsequently combined with 3  $\mu$ l 10X buffer (buffer 3, New England BioLabs), 1  $\mu$ l BamHI (NEB), and 6  $\mu$ l distilled water, and incubated at 37° for two hours. The resultant material was purified by 15 preparative gel electrophoresis using low melting point agarose, and the band was visualized under long wave ultraviolet light and excised from the gel. The gel slice was treated with Gelase using conditions recommended by the manufacturer (Epicentre Technologies). The resulting DNA 20 pelled was resuspended in 25-50  $\mu l$  of 10 mM TRIS-CL (pH 8.0) and 1 mM EDTA (TE). An aliquot of this material was ligated into the Pet9c expression vector (Dunn, J. J. et al., Protein Expression and Purification 1: 159 (1990)).

To ligate the material into the Pet9c expression vector, 20-50 ng of pl2 nucleic acid sequences cut and purified as described above was combined with 5  $\mu$ l 10 One-Phor-All (OPA) buffer (Pharmacia), 30-60 ng Pet9c cut with NdeI and BamHI, 2.5  $\mu$ l 20 mM ATP, 2  $\mu$ l T4 DNA ligase (Pharmacia) diluted 1:5 in 1% OPA buffer, and sufficient distilled water to bring the final volume to 50  $\mu$ l. The mixture was incubated at 12°C overnight.

The resultant ligations were transformed into competent DH5-alpha cells and plated on nutrient agar plates containing 50  $\mu g/ml$  kanamycin and incubated

overnight at 37 °C. DH5-alpha is used as a "storage strain" for T7 expression clones, because it is RecA deficient, so that recombination and concatenation are not problematic, and because it lacks the T7 RNA polymerase gene necessary to express the cloned gene. The use of this strain allows for cloning of potentially toxic gene products while minimizing the chance of deletion and/or rearrangement of the desired genes. Other cell lines having similar properties may also be used.

10 Kanamycin resistant colonies were single-colony purified on nutrient agar plates supplemented with kanamycin at 50  $\mu$ g/ml. A colony from each isolate was inoculated into 3-5 ml of liquid medium containing 50  $\mu$ g/ml kanamycin, and incubated at 37°C without agitation.

15 Plasmid DNA was obtained from 1 ml of each isolate using a hot alkaline lysis procedure (Mantiatis, T. et al., Molecular Cloning: A Laboratory Manual, cold Spring Harbor Laboratory, Cold Spring Harbor, NY (1982)).

Plasmid DNA was digested with EcoRI and BglII in the following manner: 15  $\mu$ l plasmid DNA was combined with 2  $\mu$ l 10% buffer 3 (NEB), 1  $\mu$  EcoRI (NEB), 1  $\mu$ l BglII (NEB) and 1  $\mu$ l distilled water, and incubated for two hours at 37°C. The entire reaction mixture was electrophoresed on an analytical agarose gel. Plasmids carrying the p12 insert were identified by the presence of a band corresponding to

925 base-pairs (full length p12) or 875 base-pairs (nonlipidated p12).

One or two plasmid DNAs from the full length and nonlipidated p12 clones in Pet9c were used to transform BL21 DE3 pLysS to kanamycin resistance as described by Studier et al. (Methods in Enzymology, Goeddel, D. (Ed.), Academic Press, 185: 60-89 (1990)). One or two transformants of the full length and nonlipidated clones were single-colony purified on nutrient plates containing 25  $\mu$ g/ml chloramphenicol (to maintain pLysS) and 50  $\mu$ g/ml

kanamycin at 37 °C. One colony of each isolate was inoculated into liquid medium supplemented with chloramphenicol and kanamycin and incubated overnight at The overnight culture was subcultured the following 5 morning into 500 ml of liquid broth with chloramphenicol (25  $\mu$ g/ml) and kanamycin (50  $\mu$ g/ml) and grown with aeration at 37°C in an orbital air-shaker until the absorbance at 600 nm reached 0.4-0.7. Isopropyl-thio-galactoside (IPTG) was added to a final concentration of 0.5 mM, for induction, and the culture was incubated for 3-4 hours at 10 37° as before. The induced cells were pelleted by centrifugation and resuspended in 25 ml of 20 mM NaPO, (pH 7.7). A small aliquot was removed for analysis by gel electrophoresis. Expressing clones produced proteins which 15 migrated at the 12 kDa position.

A crude cell lysate was prepared from the culture as described for recombinant OspA by Dunn, J.J. et al., (Protein Expression and Purification 1: 159 (1990)). crude lysate was first passed over a Q-sepharose column 20 (Pharmacia) which had been pre-equilibrated in Buffer A: 10 mM NaPO4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The column was washed with 10 mM NaPO4, 50 mM NaCl and 0.5 mM PMSF and then pl2 was eluted in 10 mM NaPO4, 0.5 mM PMSF with a NaCl gradient from 50-400 mM. pl2 eluted approximately halfway through the gradient between 100 and 200 mM NaCl. The peak 25 fractions were pooled and dialyzed against 10 mM NaPo4 (pH 7.7), 10 mM NaCl, 0.5 mM PMSF. The protein was then concentrated and applied to a Sephadex G50 gel filtration column of approximately 50 ml bed volume (Pharmacia), in 10 mM NaPO, 200 mM NaCl, 0.5 mM PMSF. p12 would typically elute shortly after the excluded volume marker. Peak fractions were determined by running small aliquots of all fractions on a gel. The p12 peak was pooled and stored in small aliquots at -20°C.

# Example 4. Generation of Chimeric Nucleic Acid Sequences and Chimeric Proteins

# A. General Protocol for Creation of Chimeric Nucleic Acid Sequences

The megaprimer method of site directed mutagenesis and its modification were used to generate chimeric nucleic acid sequences (Sarkar and Sommer, <u>Biotechniques 8(4):</u> 404-407 (1990); Aiyar, A. and J. Leis, <u>Biotechniques 14(3):</u> 366-369 (1993)). A 5' primer for the first genomic

template and a 3' fusion oligo are used to amplify the desired region. the fusion primer consists of a 3' end of the first template (DNA that encodes the amino-proximal polypeptide of the fusion protein), coupled to a 5' end of the second template (DNA that encodes the carboxy-proximal polypeptide of the fusion protein).

The PCR amplifications are performed using Taq DNA polymerase, 10% PCR buffer, and MgCl $_2$  (Promega Corp., Madison, WI), and Ultrapure dNTPs (Pharmacia, Piscataway, NJ). One  $\mu g$  of genomic template 1, 5  $\mu$  of 10  $\mu M$  5' oligo

- and 5  $\mu$ l of 10  $\mu$ M fusion oligo are combined with the following reagents at indicated final concentrations: 10X Buffer-Mg FREE (1X), MgCl<sub>2</sub> (2 mM), dNTP mix (200  $\mu$ M each dNTP), Taq DNA polymerase (2.5 units), water to bring final volume to 100  $\mu$ l. A Thermal Cycler (Perkin Elmer Cetus,
- Norwalk, CT) is used to amplify under the following conditions: 35 cycles at 95°C for one minute, 55°C for two minutes, and 72° for three minutes. This procedure results in a "megaprimer".

The resulting megaprimer is run on a 1% TAE, 4% low- 30 melt agarose gel. The megaprimer band is cut from the gel and purified using the Promega Magic PCR Preps DNA purification system. Purified megaprimer is then used in a second PCR step. One  $\mu g$  of genomic template 2, approximately 0.5  $\mu g$  of the megaprimer, and 5  $\mu$  of 10  $\mu M$  3'

oligo are added to a cocktail of 10X buffer, MgCl2, dNTPs and Tag at the same final concentrations as noted above, and brought to 100  $\mu$ l with water. PCR conditions are the same as above. The fusion product resulting from this amplification is also purified using the Promega Magic PCR Preps DNA purification system.

The fusion product is then ligated into TA vector and transformed into E. coli using the Invitrogen (San Diego, CA) TA Cloning Kit. Approximately 50 ng of PCR fusion product is ligated to 50 ng of pCRII vector with 1X Ligation Buffer, 4 units of T4 ligase, and brought to 10 Nl with water. This ligated product mixture is incubated at 12°C overnight (approximately 14 hours). Two  $\mu$ l of the ligation product mixture is added to 50  $\mu$ l competent INC F' cells and 2  $\mu$  beta mercaptoethanol. The cells are then incubated for 30 minutes, followed by heat shock treatment at 42°C for 60 seconds, and an ice quenching for two minutes. 450  $\mu$ l of warmed SOC media is then added to the cells, resulting in a transformed cell culture which is incubated at 37°C for one hour with slight shaking. of the transformed cell culture is plated on LB + 50  $\mu$ g/ $\mu$ l ampicillin plates and incubated overnight at 37°C. white colonies are picked and added to individual overnight cultures containing 3 ml LB with ampicillin (50  $\mu g/\mu l$ ).

The individual overnight cultures are prepared using Promega's Magic Miniprep DNA purification system. A small amount of the resulting DNA is cut using a restriction digest as a check. DNA sequencing is then performed to check the sequence of the fusion nucleic acid sequence, 30 using the United States Biochemical (Cleveland, OH) Sequenase Version 2.0 DNA sequencing kit. Three to five  $\mu g$ of plasmid DNA is used per reaction. 2  $\mu$ l 2M NaOH/2mM EDTA are added to the DNA, and the volume is brought to 20  $\mu$ l with water. The mixture is then incubated at room temperature for five minutes. 7  $\mu$ l water, 3 $\mu$ l 3M NaÅc, 75

15

 $\mu$ l EtOH are added. The resultant mixture is mixed by vortex and incubated for ten minutes at -70°C, and then subjected to microfugation. After microfuge for ten minutes, the supernatant is aspirated off, and the pellet is dried in the speed vac for 30 second. 6  $\mu$ l water, 2  $\mu$ l annealing buffer, and 2  $\mu$ l of 10  $\mu$ M of the appropriate oligo is then added. This mixture is incubated for 10 minutes at 37°C and then allowed to stand at room temperature for 10 minutes. Subsequently, 5.5  $\mu$ l of label cocktail (described above) is added to each sample of the mixture, which are incubated at room temperature for an additional five minutes. 3.5  $\mu$ l labeled DNA is then added to each sample which is then incubated for five minutes at 37°C. 4  $\mu$ l stop solution is added to each well. The DNA is denatured at 95° for two minutes, and then placed on ice.

Clones with the desired fusion nucleic acid sequences are then recloned in frame in the pEt expression system in the lipidated (full length) and non-lipidated (truncated, i.e., without first 17 amino acids) forms. The product is amplified using restriction sites contained in the PCR primers. The vector and product are cut with the same enzymes and ligated together with T4 ligase. The resultant plasmid is transformed into competent E. coli using standard transformation techniques. Colonies are screened as described earlier and positive clones are transformed into expression cells, such as E. coli BL21, for protein expression with IPTG for induction. The expressed protein in its bacterial culture lysate form and/or purified form 30 is then injected in mice for antibody production. The mice are bled, and the sera collected for agglutination, in vitro growth inhibition, and complement- dependent and independent lysis tests.

# B. Specific Chimeric Nucleic Acid Sequences

Various chimeric nucleic acid sequences were generated. The nucleic acid sequences are described as encoding polypeptides from Borrelia proteins. The chimeric nucleic acid sequences are produced such that the nucleic acid sequence encoding one polypeptide is in the same reading frame as the nucleic acid sequence encoding the next polypeptide in the chimeric protein sequence encoded by the chimeric nucleic acid sequence. The proteins are listed sequentially (in order of presence of the encoding 10 sequence) in the description of the chimeric nucleic acid sequence. For example, if a chimeric nucleic acid sequence consists of bp 1-650 from OspA-1 and bp 651-820 from OspA-2 were sequenced, the sequence of the chimer would include 15 the first 650 base pairs from OspA-1 followed immediately by base pairs 651-820 of OspA-2.

OspA-K48/OspA-PGau A chimer of OspA from strain K48 (OspA-K48) and OspA from strain PGau (OspA-PGau) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-654 from OspA-K48, followed by bp 655-820 from OspA-PGau. Primers used included: the amino-terminal sequence of OspA primer #607 (SEQ ID NO. 16); the fusion primer,

5'-AAAGTAGAAGTTTTTGAATCCCATTTTCCAGTTTTTT-3' (minus strand primer #668-654) (SEQ ID NO. 84); the carboxy-terminal sequence of OspA primer #586 (SEQ ID NO. 19); and the sequence primers #369 (SEQ ID NO. 14) and #357 (SEQ ID NO. 15). The chimeric nucleic acid sequence is presented as SEQ ID NO. 85; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 86.

OspA-B31/OspA-PGau A chimer of OspA from strain B31 (OspA-B31) and OspA from strain PGau (OspA-PGau) was generated

using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-PGau. Primers used included: the fusion primer,

5'-AAAGTAGAAGTTTTTGAATTCCAAGCTGCAGTTTT-3' (minus strand primer #668-651) (SEQ ID NO. 87); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence is presented as SEQ ID NO. 88; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 89.

OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-K48. Primers used included: the

15 bp 652-820 from OspA-K48. Primers used included: the fusion primer,

5'-AAAGTGGAAGTTTTTGAATTCCAAGCTGCAGTTTTTTT-3' (minus strand primer #671-651) (SEQ ID NO. 90); and the sequence primer, #369 (SEQ ID NO. 14). The chimeric nucleic acid sequence is presented as SEQ ID NO. 91; the chimeric protein encoded

by this chimeric nucleic acid sequence is presented as SEQ ID NO. 92.

OspA-B31/OspA-25015 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain 25015 (OspA-25015) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspA-25015. Primers used included: the fusion primer, 5'-TAAAGTTGAAGTGCCTGCATTCCAAGCTGCAGTTT-3' (SEQ ID NO. 93). The chimeric nucleic acid sequence is presented as SEQ ID NO. 94; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 95.

OspA-K48/OspA-B31/OspA-K48 A chimer of OspA from strain B31 (OspA-B31) and OspA from strain K48 (OspA-K48) was generated using the method described above. This chimeric nucleic acid sequence included bp 1-570 from OspA-B31, followed by bp 570-651 from OspA-B31, followed by bp 650-820 from OspA-K48. Primers used included: the fusion primer, 5'-CCCCAGATTTTGAAATCTTGCTTAAAACAAC-3' (SEQ ID NO.96); and the sequence primer, #357 (SEQ ID NO.15). The chimeric nucleic acid sequence is presented as SEQ ID NO.97; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO.98.

OSDA-B31/OSDA-K48/OSDA-B31/OSDA-K48

A chimer of OSDA
from strain B31 (OSDA-B31) and OSDA from strain K48 (OSDAK48) was generated using the method described above. This
chimeric nucleic acid sequence included bp 1-420 from OSDAB31, followed by 420-570 from OSDA-K48, followed by bp 570650 from OSDA-B31, followed by bp 651-820 from OSDA-K48.
Primers used included: the fusion primer, 5'CAAGTCTGGTTCCAATTTGCTCTTGTTATTAT-3' (minus strand primer

20 #436-420) (SEQ ID NO. 99); and the sequence primer, #357
(SEQ ID NO. 15). The chimeric nucleic acid sequence is
presented as SEQ ID NO. 100; the chimeric protein encoded
by this chimeric nucleic acid sequence is presented as SEQ
ID NO. 101.

OspA-B31/OspB-B31 A chimer of OspA and OspB from strain B31 (OspA-B31, OspB-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-651 from OspA-B31, followed by bp 652-820 from OspB-B31. Primers used included: the fusion primer, 5'-GTTAAAGTGCTAGTACTGTCATTCCAAGCTGCAGTTTTTTT-3' (minus strand primer #740-651) (SEQ ID NO. 102); the carboxy-terminal sequence of OspB primer #1106 (SEQ ID NO. 25); and the sequence primer #357 (SEQ ID NO. 15). The chimeric

nucleic acid sequence is presented as SEQ ID NO. 103; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 104.

OspA-B31/OspB-B31/OspC-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-650 from OspA-B31, followed by bp 652-820 from OspB-B31, followed by bp 74-630 of OspC-B31. Primers used included: the fusion primer, 5'-TGCAGATGTAATCCCATCCGCCATTTTTAAAGCGTTTTT-3' (SEQ ID NO. 105); and the carboxy-terminal sequence of OspC primer (SEQ ID NO. 28). The chimeric nucleic acid sequence is presented as SEQ ID NO. 106; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 107.

OspC-B31/OspA-B31/OspB-B31 A chimer of OspA, OspB and OspC from strain B31 (OspA-B31, OspB-B31, and OspC-B31) was generated using the method described above. The chimeric nucleic acid sequence included bp 1-630 from OspC-B31, followed by bp 52-650 from OspA-B31, followed by bp 650-820 of OspB-B31. Primers used included: the amino-terminal sequence of OspC primer having SEQ ID NO. 27; the fusion primer, 5'-GCTGCTAACATTTTGCTTAGGTTTTTTTGGACTTTC-3' (minus strand primer #69-630) (SEQ ID NO. 108); and the sequence primers #520 (SEQ ID NO. 40) and #200 (SEQ ID NO. 18). The chimeric nucleic acid sequence is presented as SEQ ID NO. 109; the chimeric protein encoded by this chimeric nucleic acid sequence is presented as SEQ ID NO. 110.

### 30 Additional Chimeric Nucleic Acid Sequences

Using the methods described above, other chimeric nucleic acid sequences were produced. These chimeric

nucleic acid sequences, and the proteins encoded, are summarized in Table 3.

Table III Chimeric Nucleic acid Sequences and the Encoded Proteins

Chimers Generated (base pairs)	SEQ ID NO. (nt)	SEQ ID NO. (protein) .
OspA (52-882) / p93 (1168-2100)	111	112
OspB (45-891) / p41 (122-234)	113	114
OspB (45-891) / p41 (122-295)	115	116
OspB (45-891) / p41 (140-234)	117	118
OspB (45-891) / p41 (140-295)	119	120
OspB (45-891) / p41 (122-234) / OspC (58-633)	121	122
OspA-Tro/OspA-Bo	137	138
OspA-PGau/OspA-Bo	139	140
OspA-B31/OspA-PGau/OspA-B31/ OspA-K48	141	142
OspA-PGau/OspA-B31/OspA-K48	143	144

# C. Purification of Proteins Generated by Chimeric Nucleic Acid Sequences

The chimeric nucleic acid sequences described above, as well as chimeric nucleic acid sequences produced by the methods described above, are used to produce chimeric proteins encoded by the nucleic acid sequences. Standard methods, such as those described above in Example 3, concerning the expression of proteins from Borrelia genes, can be used to express the proteins in a compatible host organism. The chimeric proteins can then be isolated and purified using standard techniques.

If the chimeric protein is soluble, it can be purified on a Sepharose column. Insoluble proteins can be solubilized in guanidine and purified on a Ni++ column;

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alternatively, they can be solubilized in 10 mM NaPO<sub>4</sub> with 0.1 - 1% TRIXON X 114, and subsequently purified over an S column (Pharmacia). Lipidated proteins were generally purified by the latter method. Solubility was determined by separating both soluble and insoluble fractions of cell lysate on a 12% PAGE gel, and checking for the localization of the protein by Coomasie staining, or by Western blotting with monoclonal antibodies directed to an antigenic polypeptide of the chimeric protein.

### 10 Equivalents

Those skilled in the art will recognize, or be able to ascertain using no more than routine experimentation, many equivalents to the specific embodiments of the invention described herein. such equivalents are intended to be encompassed in the scope of the following claims.

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#### CLAIMS

### What is claimed is:

- 1. A chimeric protein comprising two or more antigenic Borrelia polypeptides, wherein the antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
  - 2. The chimeric protein of Claim 1, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- The chimeric protein of Claim 2, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 4. The chimeric protein of Claim 3, wherein the antigenic Borrelia polypeptides are from corresponding proteins from two or more different species of Borrelia.
- 5. The chimeric protein of Claim 3, wherein the antigenic

  Borrelia polypeptides are from non-corresponding

  proteins from at least two different species of

  Borrelia.
- 6. The chimeric protein of Claim 1, wherein two or more antigenic Borrelia polypeptides are from the same species of Borrelia.

- 7. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 8. The chimeric protein of Claim 7, wherein the antigenic Borrelia polypeptides are from the same protein.
- 9. The chimeric protein of Claim 6, wherein the antigenic Borrelia polypeptides are from different proteins.
- 10. A chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the amino-proximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 20 11. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from the same species of Borrelia.
- 12. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
  - 13. The chimeric protein of Claim 11, wherein the first outer surface protein is outer surface protein B, and

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the second outer surface protein is outer surface protein A.

- 14. The chimeric protein of Claim 10, wherein the first and second outer surface proteins are from different species of *Borrelia*.
- 15. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 10 16. The chimeric protein of Claim 14, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 17. The chimeric protein of Claim 14, wherein the first

  15 and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 18. The chimeric protein of Claim 10, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 19. The chimeric protein of Claim 18, wherein the aminoproximal polypeptide further comprises a first,
  second, and third hypervariable domain, the first
  hypervariable domain consisting of residues 120
  through 140 of outer surface protein A, the second
  hypervariable domain consisting of residues 150
  through 180 of outer surface protein A, and the third

hypervariable domain consisting of residues 200 through 217 of outer surface protein A.

- 20. The chimeric protein of Claim 19, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- The chimeric protein of Claim 10, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
- 22. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides,

  wherein the two antigenic Borrelia polypeptides which comprise the chimeric protein do not occur naturally in the same protein in Borrelia.
- 23. The nucleic acid sequence of Claim 22, wherein the antigenic Borrelia polypeptides are from two or more different species of Borrelia.
- 24. The nucleic acid sequence of Claim 23, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 25. The nucleic acid sequence of Claim 24, wherein the antigenic Borrelia polypeptides are from corresponding

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proteins from two or more different species of Borrelia.

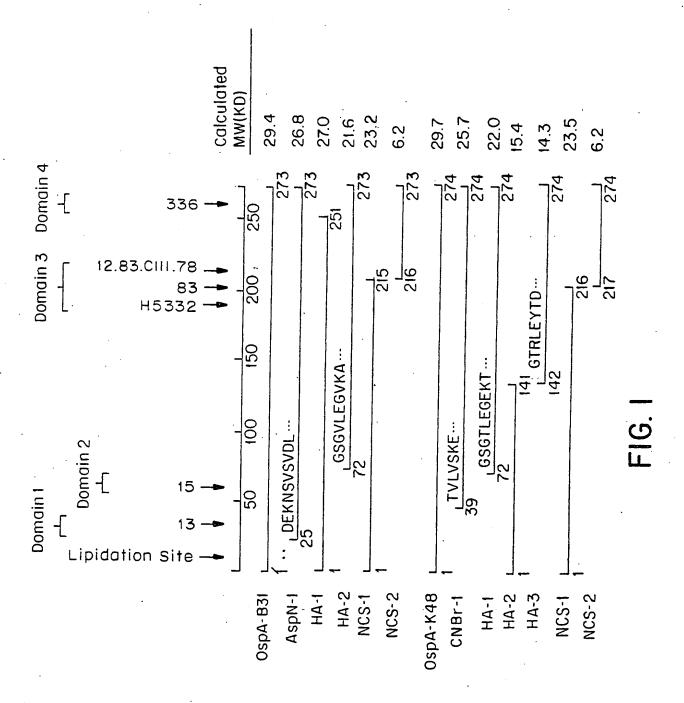
- 26. The nucleic acid sequence of Claim 24, wherein two or more of the antigenic *Borrelia* polypeptides are from non-corresponding proteins from different species of *Borrelia*.
  - 27. The nucleic acid sequence of Claim 22, wherein two or more antigenic *Borrelia* polypeptides are from the same species of *Borrelia*.
- 10 28. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are derived from Borrelia proteins selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.
  - 29. The nucleic acid sequence of Claim 28, wherein the antigenic *Borrelia* polypeptides are from the same protein.
- 30. The nucleic acid sequence of Claim 27, wherein the antigenic Borrelia polypeptides are from different proteins.

- 31. A nucleic acid sequence encoding a chimeric protein comprising two antigenic Borrelia polypeptides flanking a tryptophan residue, wherein the aminoproximal polypeptide consists of a polypeptide that is proximal from the single tryptophan residue of a first outer surface protein of Borrelia, and the carboxy-proximal polypeptide consists of a polypeptide that is distal from the single tryptophan residue of a second outer surface protein of Borrelia.
- 10 32. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from the same species of *Borrelia*.
- 33. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 34. The nucleic acid sequence of Claim 32, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
  - 35. The nucleic acid sequence of Claim 31, wherein the first and second outer surface proteins are from different species of *Borrelia*.
- 36. The nucleic acid sequence of Claim 35, wherein the
  first outer surface protein is outer surface protein A
  and the second outer surface protein is outer surface
  protein B.

- 37. The nucleic acid sequence of Claim 35, wherein the first outer surface protein is outer surface protein B, and the second outer surface protein is outer surface protein A.
- 5 38. The nucleic acid sequence of Claim 35, wherein the first and second outer surface proteins are corresponding proteins selected from the group consisting of: outer surface protein A and outer surface protein B.
- 10 39. The nucleic acid sequence of Claim 31, wherein the first outer surface protein is outer surface protein A and the second outer surface protein is outer surface protein B.
- 40. The nucleic acid sequence of Claim 39, wherein the
  amino-proximal polypeptide further comprises a first
  and a second hypervariable domain, the first
  hypervariable domain consisting of amino acid residues
  1 through 140 of outer surface protein A, and the
  second hypervariable domain consisting of amino acid
  residues 150 through 217 of outer surface protein A.
  - 41. The nucleic acid sequence of Claim 40, wherein the first and second hypervariable domains are derived from outer surface protein A from different species of Borrelia.
- 25 42. The nucleic acid sequence of Claim 31, further comprising an antigenic Borrelia polypeptide derived from a Borrelia protein selected from the group consisting of: outer surface protein A, outer surface protein B, outer surface protein C, outer surface protein D, p12, p39, p41, p66, and p93.

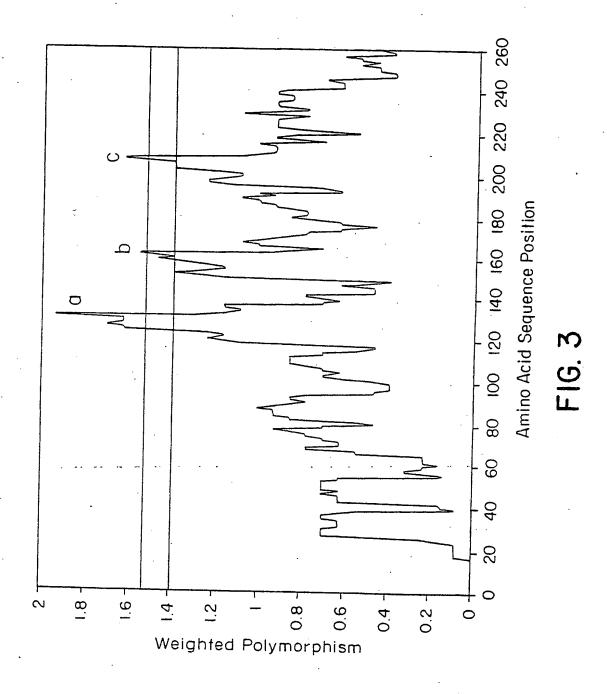
- 43. A nucleic acid sequence having a sequence selected from the group consisting of: SEQ ID NO. 85, SEQ ID NO. 88, SEQ ID NO. 91, SEQ ID NO. 94, SEQ ID NO. 97, SEQ ID NO. 100, SEQ ID NO. 103, SEQ ID NO. 106, SEQ ID NO. 109, SEQ ID NO. 111, SEQ ID NO. 113, SEQ ID NO. 115, SEQ ID NO. 117, SEQ ID NO. 119, SEQ ID NO. 121, SEQ ID NO. 137, SEQ ID NO. 139, SEQ ID NO. 141, and SEQ ID NO. 143.
- 44. A protein having an amino acid sequence selected from the group consisting of: SEQ ID NO. 86, SEQ ID NO. 89, SEQ ID NO. 92, SEQ ID NO. 95, SEQ ID NO. 98, SEQ ID NO. 101, SEQ ID NO. 104, SEQ ID NO. 107, SEQ ID NO. 110, SEQ ID NO. 112, SEQ ID NO. 114, SEQ ID NO. 116, SEQ ID NO. 118, SEQ ID NO. 120, SEQ ID NO. 122, SEQ ID NO. 138, SEQ ID NO. 140, SEQ ID NO. 142, and SEQ ID NO. 144.
- 45. A chimeric protein according to any one of claims 1 to 21 and 44 for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 46. A chimeric protein according to claim 45, wherein the immunodiagnostic assay is a dot blot, Western blot, ELISA or agglutination assay.

- 47. Use of the chimeric protein according to any one of claims 1 to 21 and 44, or the nucleic acid sequence of any one of claims 22 to 43, for the manufacture of a compound for use in therapy or diagnosis, for example as a vaccine against <u>Borrelia</u> infection, in immunodiagnostic assays to detect the presence of antibodies to <u>Borrelia</u> or to measure T-cell reactivity.
- 48. Use according to claim 47, wherein the
  immunodiagnostic assay is a dot blot, Western blot,
  ELISA or agglutination assay.



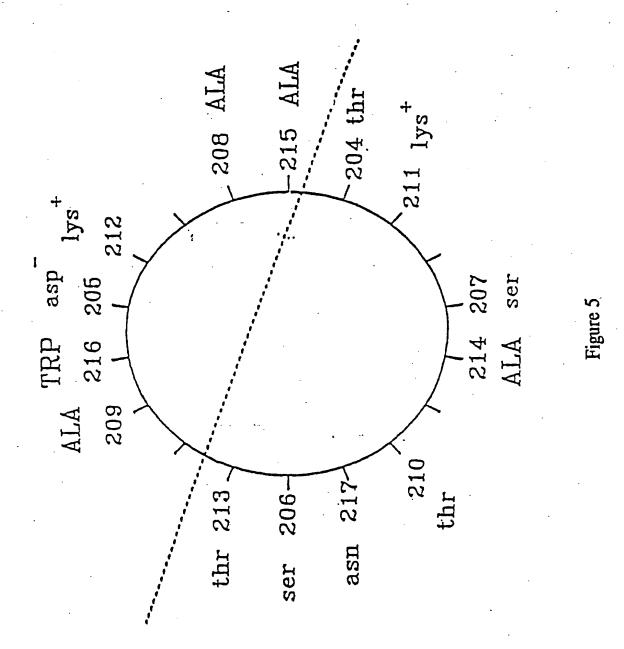
				Doil	Domain 1	_								Domain	ain 2	~`				
	34	35	36	37	38	39	40	41		65	99	67	68	69	70	7.1	72	73	74	75
A-B31	ı	а	ဗ	ធ	Σ	×	>	L	A-B31	ប	E	S	Q	×	z	z	ຍ	S	ຍ	>
A-TRO	1	Q,	ຶ	ឆ	Σ	×	>	L	A-TRO	v	L	S	D	×	တ	z	ט	လ	Ŋ	T
Λ-K48	'n	Ġ,	ტ	ט ٔ	Σ	T	>	:1	A-K48	ย	H	လ	Q	¥	z	z	ຍ	S	r.	Ħ
A-DK29	1	ы	ບ	ีซ	Σ	H	>	L	A-DK29	છ	Ħ	S	Ω	ᅩ	z	z	Ö	හ	ຍ	E
A-P/Gau	IJ	ď	ບ	M	Σ	×	>	ı	A-P/Gau	Ð	H	ຶ່	D	×	Ω	z	ຍ	Ŋ	ຍ	T
A-PKo	H	, بھ	ບ	ធ	Σ	×	>	រា	A-PKo	೮	₽⊣	S	D	×	Q	Z	ව	S	ຍ	H
A-IP3	בי	а	ຶ	臼	н	×	>	1	A-IP3	೮	H	ស	Ω	×	Ω	Z	ഇ	လ	ບ	>
A-IP90	J	ф	ប	೮	Σ	೮	>	J.	A-IP90	Ð	. [4	က	Q	×	z	z	ಶ	Ŋ	ຶ	H
A-25015		Д	9	লে	Σ	×	>	ı	A-25015	, v	F	S	Q	×	Z	z	ဗ	S	Ö	>
			Ō	Domain	m	-					_	Domain 4	4							
	1 90		200	c		210		770		5										
,		5			9	7		0 10	1	007	•	790		7/0						
A-B31	NIN	KSGE	NISKSGEVSVELNDTDSSAATKKTAAWNSGT	LNDI	DSSA	ATKK	TAAW	NSGT	A-B31	SNGTKLEGSAVEITKLDEIKN	EGS	AVEIT	CKLD	SIKN						
A-TRo	HIE	NSGE	HIPNSGEITVELNDSNSTQATKKTGKWDSNT	LINDS	NSTQ	ATKK	TGKW	DSNT	A-TRO	SAGINLEGNAVEIKTLDELKN	EGN	AVEIR	CTLD	3LKN						
A-K48	NIL	KSGE	NILKSGEITVALDDSDTTQATKKTGKWDSKT	rdds	DTTQ	ATKK	TGKW	DSKT	A-K48	SAGTNLEGKAVEITTLKELKN	EGK	WEIT	TLK	SLKN						
A-DK29	NIL	KSGE	NILKSGEITAALDDSDTTRATKKTGKWDSKT	rdds	DTTR	ATKK	TGKW	DSKT	A-DK29	SAGTNLEGKAVEITTLKELKN	EGK	AVEIT	TLKE	LKN						
A-P/Gau	EIA	KSGE	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	LNDI	NTTQ	ATKK	TGAW	DSKT	A-P/Gau	SAGTNLEGTAVEIKTLDELKN	EGT	WEIF	TLDE	SLKN						
A-PKo	EIA	KSGE	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	LNDT	NTTO	ATKK	TGAW	DSKT	A-PKo	SAGTNLEGTAVEIKTLDELKN	EGT	WEIF	TLDE	3LKN						
A-IP3	EIA	KSGE	EIAKSGEVTVALNDTNTTQATKKTGAWDSKT	LNDT	NTTQ	ATKK	TGAW	DSKT	A-IP3	SAGTNLEGTAVEIKTLDELKN	EGT	VEIR	TLDE	ZLKN						
A-IP90	HIS	NSGE	HISNSGEITVELNDSDTTQATKKTGTWDSKT	LNDS	DTTQ	ATKK	rgtw	DSKT	A-IP90	SAGTNLEGKAVEITTLKELKN	EGK	VEIT	TLKE	SLKN					,	
A-25015	HIS	KSGE	HISKSGEVTAELNDTDSTQATKKTGKWDAGT	LNDT	DSTQ	ATKK.	rgkwi	DAGT	A-25015	SAGTNLEGTAVEIKTLDEIKN	EGT	VEIR	TLDE	IKN	-					

Figure



ELNDTDSSAATKKTAAWNSGT	ALDDSOTTQATKKTGKWDSKT		ELND <u>s</u> d <u>i</u> saatkktaawnsgt	ELNOTOSSAATKKT <u>GK</u> WNSGT	ELNDTDSSAATKKTAAW <u>D</u> S <u>k</u> t	: ELND <u>s</u> d <u>i</u> saatkkt <u>gk</u> hnsgt	: ELNDSDISAATKKTAAWDSKT
B31:	K48:	٠,	613:	625:	640:	613/625:	613/640:

figure '



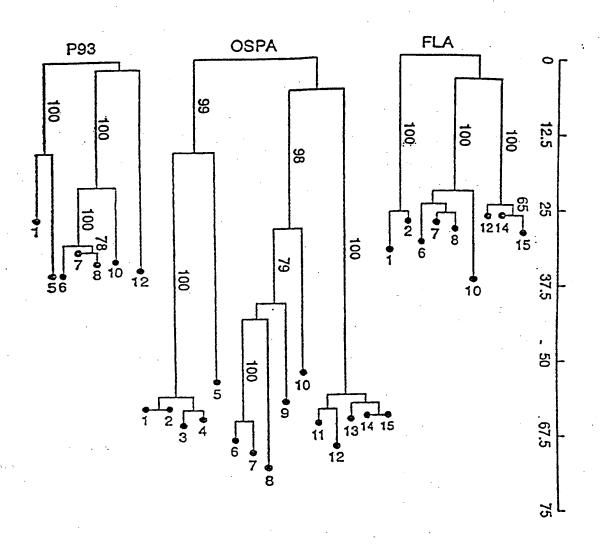


Figure 6

ATC Met	Lys	A AA	A TA:	r TT! r Let	A TTG Leu	GGA Gly	ATA Ile	GC1	CTA Leu 10	ı Ile	A TTI	A GC	C TT. a Le	A AT II u I	A GCA e Ala 5	. <b>4</b> :
TGT	Lys	G CAI	A AAT A Asi 20	o Val	AGC Ser	AGC Ser	CTI	GAC Asp 25	Glu	AAA Lys	AA A	n Sei	C GT: Va:	l Se	A GTA r Val	90
GAT <b>A</b> sp	TTG	CCI Pro 35	CT3	GAA Glu	ATG Met	AAA Lys	GTT Val 40	. Leu	GTA Val	AGC Ser	AAA Lys	GAZ Glu 45	Ly:	A AA( S As)	C AAA n Lys	144
GAC Asp	GGC Gly 50	TAE	TAC	C GAT	CTA Leu	ATT Ile 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	Lys 60	Leu	GAC	CT:	r AAA 1 Lys	192
GGA Gly 65	ACT	TCT	GAT Asp	AAA Lys	AAC Asn 70	AAT Asn	GGA Gly	TCT	GGA Gly	GTA Val 75	Leu	GAA Glu	GGC	GTA Val	AAA Lys 80	240
GCT Ala	GAC	AAA Lys	AGT Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	ATT Ile 90	TCT Ser	GAC Asp	GAT Asp	CTA Leu	GGT Gly 95	CAA Gln	288
ACC Thr	ACA Thr	CTT	GAA Glu 100	val	TTC Phe	AAA Lys	GAA Glu	GAT Asp 105	GGC Gly	AAA Lys	ACA Thr	CTA Leu	GTA Val 110	Ser	AAA Lys	336
AAA Lys	GTA Val	ACT Thr 115	TCC Ser	AAA Lys	GAC Asp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAA Lys 125	TTC Phe	AAT Asn	GAA Glu	384
AAA Lys	GGT Gly 130	GAA Glu	GTA Val	TCT Ser	GAA Glu	AAA Lys 135	ATA Ile	ATA Ile	ACA Thr	AGA Arg	GCA Ala 140	GAC Asp	GGA Gly	ACC Thr	AGA Arg	432
CTT Leu L45	GAA Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile 150	AAA Lys	AGC Ser	GAT Asp.	GGA Gly	TCT Ser 155	Gly	AAA Lys	GCT Ala	AAA Lys	GAG Glu 160	480
TT al	TTA Leu	AAA Lys	GGC Gly	TAT Tyr 165	GTT Val	CTT Leu	GAA Glu	Gly	ACT Thr 170	CTA Leu	ACT Thr	GCT Ala	GAA Glu	AAA Lys 175	ACA Thr	528
CA hr	TTG Leu	GTG Val	GTT Val 180	AAA Lys	GAA Glu	GGA . Gly '	ACT Thr	GTT Val 185	ACT Thr	TTA Leu	AGC Ser	Lys	AAT Asn 190	ATT Ile	TCA Ser	576
AA ys	Jer	GGG Gly 195	GAA Glu	GTT Val	TCA Ser	GTT ( Val (	GAA Glu 200	CTT Leu	AAT Asn	GAC Asp	Thr	GAC Asp 205	AGT Ser	AGT Ser	GCT Ala	624

Figure 7 (1 of 2)

Ala	Thr 210	Lys	Lys	Thr	Ala	Ala 215	Trp	Asn	Ser	Gly	Thr 220	Ser	Thr	Leu	ACA Thr	672
ATT Ile 225	ACT Thr	GTA Val	AAC Asn	AGT Ser	AAA Lys 230	AAA Lys	ACT Thr	AAA Lys	GAC Asp	CTT Leu 235	GTG Val	TTT Phe	ACA Thr	AAA Lys	GAA Glu 240	720
AAC Asn	ACA Thr	ATT Ile	ACA Thr	GTA Val 245	CAA Gln	CAA Gln	TAC Tyr	GAC Asp	TCA Ser 250	AAT Asn	GGC	ACC Thr	AAA Lys	TTA Leu 255	GAG Glu	768
GGG Gly	TCA Ser	GCA Ala	GTT Val 260	GAA Glu	ATT Ile	ACA Thr	AAA Lys	CTT Leu 265	GAT Asp	GAA Glu	ATT Ile	AAA Lys	AAC Asn 270	GCT Ala	TTA Leu	816
AAA	TA															822

Figure 7 (2 of 2)

OSPA K48

ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala>

50 60 70 80 90

TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAT AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val>

100 110 120 130 140

GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys>

150 160 170 180 190

GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT ASP Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys>

200 210 220 230 240

GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA AAA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys>

250 260 270 280

ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Gln>

290 300 310 320 330

ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys>

340 350 360 370 380

AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TTT CTG TTC AGT AGT TGT CTT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 8 (1 of 3)

OSP A K48

	390			40	0		4	10			420			4	30
•	•		•		•	•		•		•	•	•	•		•
AAG	GGT	GAA	ACA	TCT	GAA	AAA	ACA	ATA	GTA	AGA	GCA	AAT	GGA	ACC	AGA
TTC	CCA	CTT	TGT	AGA	CTT	TTT	TGT	TAT	CAT -	TCT	CGT	TTA	CCT	TGG	TCT
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
											•				
	4	40			450			46	50		4	170			480
•				*	•				•	~~~		•		•	•
												AAA			
												TTT			Glu>
reu	GIU	IYE	inr.	ASD	115	Lys	Ser	ASD	GIY	Ser	GIĀ	Lys	Ald	rys	CIA>
		49	90		•	500			510			52	20		
	*		*	*		•		•	•		•		•	•	
GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGA	ACT	CTA	GCT	GCT	GAC	GGC	AAA
CAA	AAT	TTT	CTG	AAA	TGA	GAA	CTT	CCT	TGA	GAT	CGA	CGA	CTG	CCG	TTT
Val	Leu	Lys	Asp	Phe	Thr	Leu	Glu	Gly	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
530			540			55	50		-	60			570		
*		*	•		•		*			-		•	•		•
												AGC			
												TCG			TAA Ile>
1111	7 117	Den	Lys	AGI	1111	Giu	Gly	1111	VGI	AGI	Den	ser	Lys	Asn	116>
51	во			590			600			61	.0			520	
•	•	•		*		•	•		•		*	•		•	
TTA	AAA	TCC	GGA	GAA	ATA	ACA	GTT	GCA	CTT	GAT	GAC	TCT	GAC	ACT	ACT
	TIT	ACC	<b>CCT</b>	CTT	TAT	TGT	CAA	CGT	GAA	CTA	CTG	AGA	CTG	TGA	
															en to
Leu	Lys										Asp	Ser			Tnr>
Leu				Glu	Ile		Val	Ala						Thr	
Leu	Lys 630			Glu			Val				Asp			Thr	TDF>
•	630	Ser	Gly	Glu 6	Ile	Thr	Val	Ala 550	Leu	Asp	660	Ser	Asp	Thr	70
÷ CAG	630 •	Ser	Gly	Glu 6	Ile 40 * ACT	Thr GGA	Val	Ala 550 TGG	Leu GAT	Asp • TCA	660 *	Ser	Asp • TCC	Thr 67 ACT	70 • TTA
• CAG GTC	630 GCT CGA	Ser ACT TGA	Gly AAA TTT	Glu 6 AAA TTT	Ile 40 * ACT TGA	Thr GGA CCT	Val	Ala 50 TGG ACC	Leu GAT CTA	Asp • TCA AGT	660 * AAA TTT	Ser ACT TGA	Asp TCC AGG	Thr 67 ACT TGA	70 • TTA AAT
• CAG GTC	630 GCT CGA	Ser ACT TGA	Gly AAA TTT	Glu 6 AAA TTT	Ile 40 * ACT TGA	Thr GGA CCT	Val	Ala 50 TGG ACC	Leu GAT CTA	Asp • TCA AGT	660 * AAA TTT	Ser ACT TGA	Asp TCC AGG	Thr 67 ACT TGA	70 • TTA
• CAG GTC	630 GCT CGA Ala	Ser ACT TGA	Gly AAA TTT	Glu 6 AAA TTT	Ile 40 * ACT TGA	Thr GGA CCT	Val	Ala 50 TGG ACC Trp	Leu GAT CTA	Asp • TCA AGT	AAA TTT Lys	Ser ACT TGA	Asp TCC AGG	Thr 67 ACT TGA	70 • TTA AAT
• CAG GTC	630 GCT CGA Ala	Ser ACT TGA Thr	Gly AAA TTT	Glu 6 AAA TTT	Ile 40 * ACT TGA Thr	Thr GGA CCT	Val	Ala 50 TGG ACC Trp	GAT CTA Asp	Asp • TCA AGT	AAA TTT Lys	Ser ACT TGA Thr	Asp TCC AGG	Thr 67 ACT TGA	TTA AAT Leu>
CAG GTC Gln	GCT CGA Ala	ACT TGA Thr 680	AAA TTT Lys	Glu 6 AAA TTT Lys 4 AAT	Ile 40 ACT TGA Thr 690 AGC	Thr GGA CCT Gly	AAA TTT Lys	Ala 550 TGG ACC Trp 70	GAT CTA Asp	* TCA AGT Ser  AAC	AAA TTT Lys	ACT TGA Thr 710	TCC AGG Ser	Thr 67 ACT TGA Thr .	TTA AAT Leu> 720
CAG GTC Gln ACA	630 GCT CGA Ala ATT	ACT TGA Thr 680 AGT	AAA TTT Lys GTG CAC	Glu 6 AAA TTT Lys AAT TTA	Ile  40  ACT TGA Thr  690  AGC TCG	GGA CCT Gly CAA GTT	AAA TTT Lys AAA TTT	Ala 550 TGG ACC Trp 70 ACC	GAT CTA Asp	* TCA AGT Ser AAC TTG	AAA TTT Lys CTT GAA	ACT TGA Thr 710 GTA CAT	TCC AGG Ser TTC AAG	Thr 67 ACT TGA Thr ACA TGT	TTA AAT Leu> 720 AAA TTT
CAG GTC Gln ACA	630 GCT CGA Ala ATT	ACT TGA Thr 680 AGT	AAA TTT Lys GTG CAC	Glu 6 AAA TTT Lys AAT TTA	Ile  40  ACT TGA Thr  690  AGC TCG	GGA CCT Gly CAA GTT	AAA TTT Lys AAA TTT	Ala 550 TGG ACC Trp 70 ACC	GAT CTA Asp	* TCA AGT Ser AAC TTG	AAA TTT Lys CTT GAA	ACT TGA Thr 710 GTA CAT	TCC AGG Ser TTC AAG	Thr 67 ACT TGA Thr ACA TGT	TTA AAT Leu> 720
CAG GTC Gln ACA	630 GCT CGA Ala ATT	ACT TGA Thr 680 AGT TCA Ser	AAA TTT Lys GTG CAC Val	Glu 6 AAA TTT Lys AAT TTA	ACT TGA Thr 690 AGC TCG Ser	GGA CCT Gly CAA GTT Gln	AAA TTT Lys AAA TTT	Ala 550 TGG ACC Trp 70 ACC	GAT CTA Asp 00 * AAA TTT Lys	* TCA AGT Ser AAC TTG	AAA TTT Lys CTT GAA	ACT TGA Thr 710 GTA CAT Val	TCC AGG Ser TTC AAG Phe	Thr 67 ACT TGA Thr ACA TGT	TTA AAT Leu> 720 AAA TTT
CAG GTC Gln ACA	630 GCT CGA Ala ATT	ACT TGA Thr 680 AGT TCA Ser	AAA TTT Lys GTG CAC	Glu 6 AAA TTT Lys AAT TTA	ACT TGA Thr 690 AGC TCG Ser	GGA CCT Gly CAA GTT	AAA TTT Lys AAA TTT	Ala 550 TGG ACC Trp 70 ACC	GAT CTA Asp	* TCA AGT Ser AAC TTG	AAA TTT Lys CTT GAA	ACT TGA Thr 710 GTA CAT Val	TCC AGG Ser TTC AAG	Thr 67 ACT TGA Thr ACA TGT	TTA AAT Leu> 720 AAA TTT
CAG GTC Gln ACA TGT	GCT CGA Ala ATT TAA Ile	ACT TGA Thr 680 AGT TCA Ser	AAA TTT Lys GTG CAC Val	Glu 6 AAA TTT Lys AAT TTA ASn	Ile  40  ACT TGA Thr  690  AGC TCG Ser	GGA CCT Gly CAA GTT Gln	AAA TTT Lys AAA TTT Lys	Ala 550 TGG ACC Trp 70 ACC TGG Thr	GAT CTA Asp 00 * AAA TTT Lys	* TCA AGT Ser AAC TTG Asn	AAA TTT Lys CTT GAA Leu	ACT TGA Thr 710 GTA CAT Val	TCC AGG Ser TTC AAG Phe	ACT TGA Thr ACA TGT Thr	TTA AAT Leu> 720 AAA TTT Lys>
CAG GTC Gln ACA TGT Thr	GAC	ACT TGA Thr 680 AGT TCA Ser 7	AAA TTT Lys GTG CAC Val	Glu 6 AAA TTT Lys AAT TTA ASn ACA	Ile  40  ACT TGA Thr  690  AGC TCG Ser	GGA CCT Gly CAA GTT Gln 740	AAA TTT Lys AAA TTT Lys	Ala 550 TGG ACC Trp 70 ACC TGG Thr	GAT CTA Asp 0 . AAA TTT Lys 750 . GAC	* TCA AGT Ser AAC TTG Asn	AAA TTT Lys CTT GAA Leu	ACT TGA Thr 710 GTA CAT Val	TCC AGG Ser TTC AAG Phe	ACT TGA Thr ACA TGT Thr	TTA AAT Leu> 720 AAA TTT Lys>
CAG GTC Gln ACA TGT Thr	GAC	ACT TGA Thr 680 AGT TCA Ser 7	AAA TTT Lys GTG CAC Val	Glu 6 AAA TTT Lys AAT TTA ASn ACA TGT	Ile  40  ACT TGA Thr  690  AGC TCG Ser  GTA CAT	GGA CCT Gly CAA GTT Gln 740	AAA TTT Lys AAA TTT Lys	Ala 550 TGG ACC TTP 70 ACC TGG Thr TAC ATG	GAT CTA ASP 0 * AAA TTT Lys 750 GAC CTG	* TCA AGT Ser AAC TTG Asn TCA AGT	AAA TTT Lys CTT GAA Leu GCA CGT	ACT TGA Thr 710 GTA CAT Val 70 GGC CCG	TCC AGG Ser  TTC AAG Phe  ACC TGG	ACT TGA Thr ACA TGT Thr AAT TTA	TTA AAT Leu> 720 AAA TTT Lys>

Osp A K-48

770 780 790 800 810

GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA Glu Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala>

OSP A K48

820

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 8 (3 of 3)

### OSP A PGAU

ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Alabou God At TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Alabou God CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT TCA GTA AGC TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT CYS Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Valbur Ilo				1	.0			20			30			4	10		
TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Alas  50 60 70 80 90  TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT TCA GTA ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Vals  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lyss  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAC CTA AAA CTG CAA TTC ATT CTG TTC TAT CTG TTT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lyss  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CTA TTT CTG TTT CTG TTA CAC AGA CTT CAC TGT TTT GAA GAC ATT CTG TTT TTT CTG TTT CTG TTA CAC AGA CCT CAC GAA CTT CAC TGT TTT CTG TTT CAC AGA CCT CAC GAA CTT CAC TGT TTT CAC AGA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT CTG TTA CAC AGA CCT CAC GAA CTT CAC AGA CTT CTA TTT CTG TTT AAT TGT TAA CGA CTG GTA GAT ACA AAA CCT TGA AGA AAT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT ACA CTA CTG TTT TAAT TCT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala ASP ASP Leu Ser Lys Ala Lys Leu Thr Ile Ala ASP ASP Leu Ser Lys ACC ACA TTC GAA CTT TTA AAA GAA GAT GGT GCC AAA ACA TTA GTG TCA AGA CTG TGT AAG CTT GAA AAT TTT CTT CTT CAC CCG TTT TGT AAT CAC AGT TCT THT THT Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAC ACA AGT AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TTC AGA GTT CTT TTA AGT TTC ATT CAT TCA AGA TCT CTG TTT TGT AGT TTA CTT TTA AGT TTC ATT TCA TCA AGA TCT CTG TTT TGT AGT TTA CTT TTA AGT TTC ATT CAT TCA AGA TCT CTG TTT TGT AGT TCT TTT TTT TTT TTT TTT TTT TTT TTT T			•		•	◆,		•		•	•		*		•	•	
Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala>  50 60 70 80 90  TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT TCA GTA AGC GTT CGT TTA CAA TGG TGG GAA CTA CTT TTT TTG TGG CGA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GAT CAT GTA AGT AAA GAA AAA GAC AAA CTA AAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAA ATT GAG CTA AAA CTG CCA TTC ATG TCA GAT TTC CGT TGT CAT CTG TTC TAA CTC GAT TTT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CAT TTT GGI TTT GGI TTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT GGI TTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT GGI TTT GAA GAC CTA TTT TTT CTG TTT ACA AGA CCT CAC GAA CTT CCA TGT TTT AAA AGA CAT TAA CAC ATG TTT TAA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGA AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala ASP ASP Leu Ser Lys>  250 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TTA CTT TTA AGA TTA CTT TAA AGA TTA CTT TTA AGA TTC CAT TTA AGA TTC CTT TTA AGA TTC CTT TTA AGA TTC CTT TTA AGA TTC CTT TTA AGA TTC CAT TTA CTT TAA AGA TTC CAT TCA AGA TCT TCTG TTT TGT TTT TGT TTA TTT TAA TTC TTA CAT TCA AGA TTC TTT TTT TTT TTT TTT TTAT		ATG	AAA	AAA	TAT	ATT	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT TCA GTA ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT CYS LyS Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTTA AAC GAG CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAG CTA AAA CTA ATG ATG ATG ATG TTC ATG TTC ATG TTC ATG TCG TGT TGT TAT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT GLY THY Ser Asp Lys Asp Asp Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CAT CTA AGT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys Ala Lys Leu Thr Tle ATT TGT AAT CAC AGT TCT TTT TCT TTT TCT GAA AAT TTT CTT CTT TTT CTT TTT TTT TTT T																	
TGC AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA AAC AGC GCT TCA GTA ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT CYS Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAC GAA CAT TCA TTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAA TTT CAT TA ACTC GAT TTT Asp Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTT CCA AGA CCT TGA AGA CTA TTT CTG TTT CCA AGA CCT CAC GAA CTT CCA TGT TTT GRA AGA CTA TTT CTG TTT CCA AGA CCT CAC GAA CTT CCA TGT TTT CAT TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT CAT TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT ASP Lys Asp Asp Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys ACG TGT TA AGT TAA CCA CAC TTC GAA CTT GAA ATT TCTT TTT TTT TTT TTT TTT TTT TTT		met	Lys	Lys	lyr	Ten	ren	GIY	116	GLY	Dea	116	Dea	VIG	Deu	116	VION
TGC AAG CAA AT GTT AGC AGC CTT GAT GAA AAA AAA AGC GCT TCA GTA ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT CYS LYS GIN ASN Val Ser Ser Leu ASP Glu Lys ASN Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTC AAAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys ASP Lys ASP Lys ASP Lys ASP CTG CCA TTC ATG TCA AGG GAC AAA CTG CAT TTC ATG TCA AGG CGA CTC TAC AGA CAT TCC TTT CAA GTA CTG CAT TTC ATG TCA GAT TTC CGT TGT CAT CTG TCT AAC CTG GAT TTT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val ASP Lys Ile Glu Leu Lys AGG CCA ACG ATT CTG GAG AGG ACT TCT GAA GGA CTT TCT GAT CTG TCT GAA GGT ACA AAA CCT TGA AGA CTT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT CGT TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT CGT TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT ASP ASP Lys ASP ASP Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala ASP ASP Leu Ser Lys Ala Lys Leu Thr Ile Ala ASP ASP Leu Ser Lys ACG TCG TGT AAG CTT GAA AAT TCT TTT TCT TTA AAT TCT CTT TCT TTT AAT TCT TTT TCT TTT TCT TTT TCT TTT TCT TTT TCT TTT AAT TCT TTT AAT CAC AGT TCT TTT TCT TTT TTT TTT TTT TTT TTT T		50			60		•	7	0			80			90		
ACG TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTG TCG CGA AGT CAT CYS Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT CTG TTT ASP Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAG CTA AAA CTG CCA TTC ATG TCA GAT TTC CGT TGT CAT CTG TTC TAA CTC GAT TTT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT GIY Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT TAT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys-Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys-ACA CTG TGT AAG CTT GAA AAT TTT CTG TTT AAA GAA CTA CTA GTG TTT TCA TTT CGT TTT AAA GAA CTA CTA GTG TTT TCA TTT CGT TTT AAA GAA CTA CTA GTG TCA AGA CTT CTA TTT CTG TTT AAA GAA CTA CTG CTA GAT TCA TTT CTG TTT AAA GAA GAT GCT CTA GAT TCA TTT TCA TTT CGT TTT AAAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys-Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg-TTH THr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg-TTH CAT TCA AGA TCT AGA AAA TTT CAT TCA AGA TCT AAGA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAA AGA TTA CAT AGA TTT CAT TCA AGA TCT CTG TTT TGT AGT TCT TAA CGA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAA AGA TTA CTT TAA AGA TTA CTT TAA AGA TTA CAT AGA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTT TAA AGT TTA CTT TAA AGA		•		•	•		•		•	•		•		•	•		•
Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Ala Ser Val>  100 110 120 130 140  GAT TTG CCT GGT GAG ATG AAA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAC GGA CCA CTC TAC TTT CAA GAA CAT TCA TTT CTT TTT GTT TASp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150 160 170 180 190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAG CTA AAA CTG CCA TTC ATG TCA GAT TTC CGT TGT CAT CTG TTC TAA CTC GAT TTT Asp Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200 210 220 230 240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys 290 300 310 320 330 ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg> 340 350 360 370 380 AAA GTA AGT TCT AGA GAC AAA TTA GTT TCT CTA CTT TAC AAG TTA CTT TTA TTC ATT CCA TTT TGT TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT TTA TTCA TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT																	
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Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asp Lys>  150  160  170  180  190  GAC GGT AAG TAC AGT CTA AAG GCA ACA GTA GAC AAG ATT GAG CTA AAA CTG CCA TTC ATG TCA GAT TTC CGT TGT CAT CTG TTC TAA CTC GAT TTT ASP Gly Lys Tyr Ser Leu Lys Ala Thr Val Asp Lys Ile Glu Leu Lys>  200  210  220  230  240  GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250  260  270  280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290  300  310  320  330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA GAT TCT THT PHe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340  350  360  370  380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT TTA GAA ACT TCA TGT TTA AAA GAA GTA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TTT CAT TTA AGA ACA TCA ACA GAT TCA CAT TACA AGA TTA CAT TCA TTT TCA TCA TTT TCAT TCA		GAT	TTG	CCT	GGT	GAG	ATG	AAA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	AAA
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GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250  260  270  280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290  300  310  320  330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT TAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340  350  360  370  380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT TGT AGT TTT TAT AAG GTT TTT TGT AGT TTT AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT AAG TTT CAT TCA AGA TTT CAT TCA AGA TCT TTT TGT AGT TTT TAC AAG TTTA CTT		Asp	Gly	Lys	Tyr	Ser	Leu	Lys	Ala	Thr	Val	Asp	Lys	Ile	Glu	Leu	Lys>
GGA ACT TCT GAT AAA GAC AAT GGT TCT GGA GTG CTT GAA GGT ACA AAA CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250  260  270  280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290  300  310  320  330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT TAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340  350  360  370  380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT TGT AGT TTT TAT AAG GTT TTT TGT AGT TTT AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT AAG TTT CAT TCA AGA TTT CAT TCA AGA TCT TTT TGT AGT TTT TAC AAG TTTA CTT										3.	20	•		220	* .		340
CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250  260  270  280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290  300  310  320  330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340  350  360  370  380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA TCA AGA TTT CTT TGT AGT TTA CAT TCA TTT CAT TCA AGA TTT CAT TCA AGA TTT CTT TTT TGT AGT TTA AAT GAA TTT CAT TCA AGA TCT TTT TGT AGT TTA CAT TTT CAT TCA TTT TTT TGT AGT TTT TAC AAG TTT CAT TCA TTT TTT TGT AGT TTT TGT AGT TTT TAC AAG TTT CTT		•		200		•	210		•	24	*	•	•	*		•	240
CCT TGA AGA CTA TTT CTG TTA CCA AGA CCT CAC GAA CTT CCA TGT TTT Gly Thr Ser Asp Lys Asp Asn Gly Ser Gly Val Leu Glu Gly Thr Lys>  250  260  270  280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT Asp Asp Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290  300  310  320  330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340  350  360  370  380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA TCA AGA TTT CTT TGT AGT TTA CAT TCA TTT CAT TCA AGA TTT CAT TCA AGA TTT CTT TTT TGT AGT TTA AAT GAA TTT CAT TCA AGA TCT TTT TGT AGT TTA CAT TTT CAT TCA TTT TTT TGT AGT TTT TAC AAG TTT CAT TCA TTT TTT TGT AGT TTT TGT AGT TTT TAC AAG TTT CTT		GGA	ACT	TCT	GAT	AAA	GAC	AAT	GGT	TCT	GGA	GTG	CTT	GAA	GGT	ACA	AAA
250 260 270 280  GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys:  290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg:  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TCT CTA CTT TAC AAG TTA CTT		CCT	TGA	AGA	CTA	TTT	CTG	TŢA	CCA	AGA	CCT	CAC	GAA	CTT	CCA	TGT	TTT
GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys 290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg 340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		Gly	Thr	Ser	Asp	Lys	Asp	Asn	Gly	Ser	Gly	Val	Leu	Glu	Gly	Thr	Lys>
GAT GAC AAA AGT AAA GCA AAA TTA ACA ATT GCT GAC GAT CTA AGT AAA CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys 290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg 340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT				_							270						
CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT				2	50	*	•	260		•	270		•	. 2	•	•	
CTA CTG TTT TCA TTT CGT TTT AAT TGT TAA CGA CTG CTA GAT TCA TTT ASP ASP Lys Ser Lys Ala Lys Leu Thr Ile Ala Asp Asp Leu Ser Lys>  290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		GAT	GAC	AAA	AGT	AAA	GCA	AAA	TTA	ACA	ATT	GCT	GAC	GAT	CTA	AGT	AAA
290 300 310 320 330  ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT																	
ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		Asp	Asp	Lys	Ser	Lys	Ala	Lys	Leu	Thr	Ile	Ala	Asp	Asp	Leu	Ser	Lys
ACC ACA TTC GAA CTT TTA AAA GAA GAT GGC AAA ACA TTA GTG TCA AGA TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT					• .			_	• • •			220					•
TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		290			300		•	3	10			32U · •		•	330		•
TGG TGT AAG CTT GAA AAT TTT CTT CTA CCG TTT TGT AAT CAC AGT TCT Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		¥CC	. ארא	. <del>1</del> 10	GAA	CTT	TTA	AAA	GAA	GAT	GGC	AAA	ACA	TTA	GTG	TCA	AGA
Thr Thr Phe Glu Leu Leu Lys Glu Asp Gly Lys Thr Leu Val Ser Arg>  340 350 360 370 380  AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT																	
AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT																	
AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT												_					
AAA GTA AGT TCT AGA GAC AAA ACA TCA ACA GAT GAA ATG TTC AAT GAA TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		3	340	_		350			360			3	70	•			
TTT CAT TCA AGA TCT CTG TTT TGT AGT TGT CTA CTT TAC AAG TTA CTT		N N 7	ريت م	• דמג ע	, <del>പ</del> ്രഫ	ACA -	C)	_ 	מרא	ጥር ነ	ב בחב	דמה ו	י פאט. ב	יי בירות	ال <b>نگ</b>		GAA

FIGURE 9 (1 of 3)

OSP A PGAU

13/133

	200			4	^^						450				
•	390		•	4	00		•	410		•	420			4	30
AAA	GGT	GAA	TTG	тст	GCA	444	¥CC	ATG	). )	707	Ġ.a.	ልልጥ	GC N	» CC	AAA:
															TTT
Lys	Gly	Glu	Leu	Ser	Ala	Lys	Thr	Met	Thr	Arg	Glu	Asn	Gly	Thr	Lys>
. ·	•				•								_		
_		440	-	_	450			4	60			470			480
ملسلت م	CAA	ጥአጥ	202	CNN	A TO C		300	C 3 T	•	*		•		•	GAA
GAA	CTT	ATA	TGT	CTT	TAC	TTT	TCG	CTA	CÇA	TGG.	AUU. TOOT	AAA TTT	CCA	AAA	CTT
Leu	Glu	Tyr	Thr	Glu	Met	Lys	Ser	Asp	Gly	Thr	Glv	Lvs	Ala	Lvs	Glu>
								_	-		_	•		_3 -	
	_	4	90	_	:	500			510			53	20		
רדים	מידים	444	A A G	יורי ברינה ב	ልርጥ		CNA	CCV	**	CTA	-		•	•	GTA
CAA	AAT	TTT	TTC	AAA	TGA	GAA	CTT	CCT	TTT	CAT	CCA	TTA	CTA	AAA	CAT
Val	Leu	Lys	Lys	Phe	Thr	Leu	Glu	Gly	Lys	Val	Ala	Asn	ASD	Lvs	Val>
													•	-, -	
530			540	•		5	50	_	:	560			570		
ACA	TTG	GAA	GTA	<b>ΔΔΔ</b> .	GAA	GC A	yCC.	CTT.	እ <i>ር</i> ጥ	4.1.2 =	<b>&gt;</b> CT		*		•
TGT	AAC	CIT	CAT	TTT	CTT	CCT	TGG	CAA	TGA	TAA	TCA	TTC	CTT	TAA	CGT
Thr	Leu	Glu	Val	Lys	Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Glu	Ile	Ala>
÷	0.0														
- -51	80	•		590		•	600		•	61	.0	_		520	
 -51	•	•	5	590		• GTT	600		• AAT		•	• 244	•	520	
58 AAA TTT	TCT AGA	GGA CCT	GAA CTT	GTA CAT	ACA TGT	CAA	600 GCT CGA	CTT GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT	CAG GTC
58 AAA TTT	TCT AGA	GGA CCT	GAA CTT	GTA CAT	ACA TGT	CAA	600 GCT CGA	CTT GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT	CAG
58 AAA TTT	TCT AGA Ser	GGA CCT	GAA CTT	GTA CAT Val	ACA TGT Thr	CAA	GCT CGA Ala	CTT GAA Leu	TTA	GAC CTG	ACT TGA Thr	TTG	ACT TGA	ACT TGA Thr	CAG GTC Gln>
58 AAA TTT	TCT AGA	GGA CCT	GAA CTT	GTA CAT	ACA TGT Thr	CAA	GCT CGA Ala	CTT GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT	CAG GTC Gln>
AAA TTT Lys GCT	TCT AGA Ser 630	GGA CCT Gly	GAA CTT Glu	GTA CAT Val 64	ACA TGT Thr	CAA Val	GCT CGA Ala	CTT GAA Leu 550	TTA Asn TCA	GAC CTG Asp	ACT TGA Thr 660	TTG Asn TCT	ACT TGA Thr	ACT TGA Thr	CAG GTC Gln>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	GGA CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT TGA	ACA TGT Thr	CAA Val GCA CGT	600 GCT CGA Ala TGG ACC	CTT GAA Leu 550 GAT CTA	TTA ASD TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr ACT	ACT TGA Thr 67	CAG GTC Gln>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	GGA CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT TGA	ACA TGT Thr	CAA Val GCA CGT	600 GCT CGA Ala TGG ACC	CTT GAA Leu 550 GAT CTA	TTA ASD TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT	TTG Asn TCT AGA	ACT TGA Thr ACT	ACT TGA Thr 67	CAG GTC Gln>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT TGA	ACA TGT Thr 10 • GGC CCG Gly	CAA Val GCA CGT	600 GCT CGA Ala TGG ACC	CTT GAA Leu 50 GAT CTA Asp	TTA Asn TCA AGT Ser	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA Ser	ACT TGA Thr ACT	ACT TGA Thr 67 TTA AAT Leu	CAG GTC G1n> 0 • ACA TGT Thr>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	GGA CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT TGA	ACA TGT Thr	CAA Val GCA CGT	600 GCT CGA Ala TGG ACC	CTT GAA Leu 550 GAT CTA	TTA Asn TCA AGT Ser	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA	ACT TGA Thr ACT	ACT TGA Thr 67 TTA AAT Leu	CAG GTC Gln>
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu AAA TTT Lys	GTA CAT Val 64 ACT TGA Thr	ACA TGT Thr 10 • GGC CCG Gly 690 • AAA	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC TIP	CTT GAA Leu 550 GAT CTA ASP	TTA ASD TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TTG ASN TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 67 TTA AAT Leu	CAG GTC G1n> 0 ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	GGA CCT Gly AAA TTT Lys 380	GAA CTT Glu AAA TTT Lys AAC TTG	GTA CAT Val 64 ACT TGA Thr AGC TCG	ACA TGT Thr 10 GGC CCG Gly 690 AAA TTT	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC Trp	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT	TTA ASD TCA AGT Ser O	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser 10	ACT TGA Thr ACT TGA Thr ACT	ACT TGA Thr 67 TTA AAT Leu	CAG GTC G1n>  0 ACA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	GGA CCT Gly AAA TTT Lys 380	GAA CTT Glu AAA TTT Lys AAC TTG	GTA CAT Val 64 ACT TGA Thr AGC TCG	ACA TGT Thr 10 GGC CCG Gly 690 AAA TTT	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC Trp	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT	TTA ASD TCA AGT Ser O	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser 10	ACT TGA Thr ACT TGA Thr ACT	ACT TGA Thr 67 TTA AAT Leu	CAG GTC G1n> 0 ACA TGT Thr> 720
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr AGT TCA	GGA CCT Gly AAA TTT Lys 380	GAA CTT Glu AAA TTT Lys AAC TTG ASn	GTA CAT Val 64 ACT TGA Thr AGC TCG	ACA TGT Thr 10 * GGC CCG Gly 690 * AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC Trp	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT	TCA AGT Ser CAA GTT Gln	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser 10 .* TTT AAA Phe	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 67 TTA AAT Leu	CAG GTC G1n>  0 ACA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	GGA CCT Gly AAA TTT Lys 6TT CAA Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTA CAT Val 64 ACT TGA Thr AGC TCG Ser	ACA TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT Lys	GCT CGA Ala TGG ACC Trp ACT TGA Thr	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT Thr	TTA ASD TCA AGT Ser CAA GTT Gln 750	GAC CTG Asp * AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTT AGA Ser TTT AAA Phe	ACT TGA Thr ACT TGA Thr ACT	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	CAG GTC Gln>  ACA TGT Thr> 720 CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA	GGA CCT Gly AAA TTT Lys 6TT CAA Val 73	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTA CAT Val  64 ACT TGA Thr  AGC TCG Ser	ACA TGT Thr 10 *GGC CCG Gly 690 *AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT Lys	GCT CGA Ala TGG ACC Trp ACT TGA Thr	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT Thr	TTA ASD TCA AGT Ser CAA GTT Gln 750 TCC	GAC CTG Asp * AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTG ASN TCT AGA Ser 10 TTT AAA Phe	ACT TGA Thr ACT TGA Thr O	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	CAG GTC Gln>  ACA TGT Thr> 720 CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA TGT	GGA CCT Gly AAA TTT Lys 6TT CAA Val 73 ATA TAT	GAA CTT Glu AAA TTT Lys AAC TTG ASD	GTA CAT TGA Thr AGC TCG Ser GTA CAT	ACA TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT Lys 40 CAA GTT	GCT CGA Ala TGG ACC Trp ACT TGA Thr	CTT GAA Leu 50 GAT CTA ASP 70 ACA TGT Thr	TTA ASD TCA AGT Ser CAA GTT Gln 750 TCC AGG	GAC CTG Asp * AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTG ASN TCT AGA Ser 10 TTT AAA Phe 76 ACC TGG	ACT TGA Thr ACT TGA Thr TGA Thr	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	CAG GTC Gln>  ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 9 (2 of 3)

OSP A PGAU

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820
AAA TAA
TTT ATT
Lys \*\*\*>

FIGURE 9 (3 of 3)

ATG Met 1	AAA Lys	AAA Lys	TAT Tyr	TTA Leu 5	TTG Leu	GGA Gly	ATA Ile	GCT	CTA Leu 10	ATA Ile	TTA	GCT Ala	TTA Leu	ATA Ile 15	GCA Ala	4	8
TGT Cys	AAG Lys	CAA Gln	AAT Asn 20	GTT Val	AGC Ser	AGC Ser	CTT Leu	GAC Asp 25	GAG Glu	AAA Lys	AAC Asn	AGC Ser	GTT Val 30	TCA Ser	GTA Val	9	6
GAT Asp	TTG Leu	CCT Pro 35	GGT Gly	GAA Glu	ATG Met	AAA Lys	GTT Val 40	CTT Leu	GTA Val	AGC Ser	AAA Lys	GAA Glu 45	AAA Lys	GAC Asp	AAA Lys	14	4
GAC Asp	GGC Gly 50	AAG Lys	TAC Tyr	AGT Ser	CTA Leu	ATG Met 55	GCA Ala	ACA Thr	GTA Val	GAC Asp	AAG Lys 60	CTT Leu	GAG Glu	CTT Leu	AAA Lys	19:	2

Figure 10 (1 of 2)

										-,								
	GGA Gly 65	ACA Thr	TCT Ser	GAT	AAA Lys	AAC Asn 70	AAT Asn	GGA Gly	TCT	GCG	GTG Val 75	CTT Leu	GAA Glu	GGC	GTA Val	AAA Lys 80		240
	GCT Ala	Asp Asp	AAA Lys	AGC Ser	AAA Lys 85	GTA Val	AAA Lys	TTA Leu	ACA Thr	GTT Val 90	TCT Ser	GAC Asp	GAT Asp	CTA Leu	AGC Ser 95	ACA Thr		288
	ACC Thr	ACA Thr	CTT Leu	GAA Glu 100	GTT Val	TTA Leu	AAA Lys	GAA Glu	GAT Asp 105	GJÝ GGC	AAA Lys	ACA Thr	TTA Leu	GTG Val 110	TCA Ser	AAA Lys		336
	AAA Lys	AGA Arg	ACT Thr 115	TCT Ser	AAA Lys	GAT Asp	AAG Lys	TCA Ser 120	TCA Ser	ACA Thr	GAA Glu	GAA Glu	AAG Lys 125	TTC Phe	AAT Asn	GAA Glu		384
	AAA Lys	GGC Gly 130	GAA Glu	TTA Leu	GTT Val	GAA Glu	AAA Lys 135	ATA Ile	ATG Met	GCA Ala	AGA Arg	GCA Ala 140	AAC Asn	GGA Gly	ACC Thr	ATA Ile		432
	CTT Leu 145	GAA Glu	TAC Tyr	ACA Thr	GGA Gly	ATT Ile. 150	AAA Lys	AGC Ser	GAT Asp	GGA Gly	TCC Ser 155	GGA Gly	AAA Lys	GCT Ala	AAA Lys	GAA Glu 160		480
	ACT Thr	TTA Leu	AAA Lys	GAA Glu	TAT Tyr 165	GTT Val	CTT Leu	GAA Glu	GGA Gly	ACT Thr 170	CTA Leu	ACT Thr	GCT Ala	GAA Glu	AAA Lys 175	GCA Ala		528
		TTG Leu																576
		TCT Ser																624
,	GCT Ala	ACT Thr 210	AAA Lys	AAA Lys	ACT	GGG Gly	AAA Lys 215	TGG Trp	GAT Asp	GCA Ala	GGC Gly	ACT Thr 220	TCA Ser	ACT	TTA Leu	ACA Thr		672
	ATT Ile 225	ACT Thr	GTA Val	AAC Asn	AAC Asn	AAA Lys 230	AAA Lys	ACT Thr	AAA Lys	GCC Ala	CTT Leu 235	GTA Val	TTT Phe	ACA Thr	AAA Lys	CAA Gln 240		720
	GAC Asp	ACA Thr	ATT	ACA Thr	TCA Ser 245	Gln	AAA Lys	TAC Tyr	GAC Asp	TCA Ser 250	GCA Ala	GGA Gly	ACC	AAC Asn	TTG Leu 255	GAA Glu		768
	GGC Gly	ACA Thr	GCA Ala	GTC Val 260	GAA Glu	ATT	AAA Lys	ACA Thr	CTT Leu 265	GAT Asp	GAA Glu	CTT Leu	AAA Lys	AAC Asn 270	GCT Ala	TTA Leu		816
	AGA															•	•	819

Figure 10 (2 of 2)

17//33

OSP B B-31 Sequence Range: 1 to 891

30 20 10 ATG AGA TTA TTA ATA GGA TTT GCT TTA GCG TTA GCT TTA ATA GGA TGT TAC TOT AAT AAT TAT COT AAA CGA AAT CGC AAT CGA AAT TAT COT ACA Met Arg Leu Leu Ile Gly Phe Ala Leu Ala Leu Ile Gly Cys> 90 70 50 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT Ala Gln Lys Gly Ala Glu Ser Ile Gly Ser Gln Lys Glu Asn Asp Leu> 120 130 110 . 100 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG Asn Leu Glu Asp Ser Ser Lys Lys Ser His Gln Asn Ala Lys Gln Asp> 150 170 160 150 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT Leu Pro Ala Val Thr Glu Asp Ser Val Ser Leu Phe Asm Gly Asm Lys> 220 210 200 ATT TIT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT Ile Phe Val Ser Lys Glu Lys Asn Ser Ser Gly Lys Tyr Asp Leu Arg> 270 260 250 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA Ala Thr Ile Asp Gln Val Glu Leu Lys Gly Thr Ser Asp Lys Asn Asn> . . . 320 330 310 300 290 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT Gly Ser Gly Thr Leu Glu Gly Ser Lys Pro Asp Lys Ser Lys Val Lys> 360 370 350 340 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA Leu Thr Val Ser Ala Asp Leu Asn Thr Val Thr Leu Glu Ala Phe Asp> 430 390 400 410 420

FIGURE 11 (1 of 3)

•	•		•		•	•		•		• .	•		•		•
GCC	AGC	AAC	CAA	AAA	TTA	TCA	AGT	AAA	GTT	ACT	AAA	AAA	CžG	GGG	TCA
CGG	TCG	TTG	CTT	لملمك	ממד	AGT	TCA	للشك	CLL	TGA	للملمك	للملمك	670	000	AGT
פומ	500	110	Cla	Tye	710	50-	cor	Tye	Val	The	7370	Tara.	610	22	Ser>
WIG	ser	ASI	GIII	Lys	116	Sei	Ser	Lys	VG.	2 2 2 2 2	Lys	Lys	Gin	GIA	Ser>
									,						
•		140	•		450			4	50		4	170			460
•		•		•	•		•		•	•		-		•	•
ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCT	AAT	AAA	TTA	GAC	TCA	AAG	AAA	TTA
TAT	TGT	CTC	CTT	TGA.	GAG	TIT	CGA	TTA	TII	AAT	CTG	AGT	TTC	TTT	AAT
Ile	Thr	Glu	Glu	Thr	Leu	Lys	Ala	Asn	Lys	Leu	Asp	Ser	Lvs	Lvs	Leu>
•									-		-			-,-	
		49	90		5	500			510			52	20		
	•		•	•		•	_	•	•		•		•		
ביוב	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	C 4 A	מדמ	እሮኔ	C 3 C	GCT
															CGA
THI	AIG	ser	ASI	GIA	INT	Inr	reu	GIU	Tyr	Ser	Gin	lie	Thr	ASD	Ala>
		•											:		
530			540		_	5:	-			560			570		
•		*	•		, <del>"</del>			•		•		•	•		•
GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	TAA	AGC	ATT	AAG	CTT
CTG	TTA	CGA	TGT	TTT	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
Asp	Asn	Ala	Thr	Lys	Ala	Val	Glu	Thr	Leu	Lys	Asn	Ser	Ile	Lys	Leu>
														_	
51	80		5	590			600			61	10		€	20	
	•	*		•		•	•		•		•	•		•	
~	CCA	1 CM	-	C	000	~~`		101	101	CTC	~				
GAA	SOL	AG I	CII	GTA	GIL	GGA	AAA	ACA	ACA	616	GAA	ATT	AZZ	GAL	CCT
CTT	CCT	TCA	GAA	GTA CAT	CAG	CCT	TTT	TGT	TGT	CYC	CTT	TAA	AAA	GAA	GGT
CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TIT	CTT	CCA
CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TIT	CTT	GGT CCA Gly>
CTT	CCT	TCA	GAA	CAT Val	CAG Val	CCT	TTT Lys	TGT Thr	TGT	CAC	CTT Glu	TAA	TIT	CTT Glu	CCA Gly>
CTT	CCT	TCA	GAA	CAT Val	CAG	CCT	TTT Lys	TGT	TGT	CAC	CTT	TAA	TIT	CTT	CCA Gly>
CTT Glu	Gly 630	TCA Ser	GAA Leu	CAT Val	CAG Val	CCT Gly	TTT Lys	TGT Thr	TGT	CAC Val	CTT Glu 660	TAA Ile	TTT Lys	CTT Glu 67	CCA Gly>
CTT Glu •	Gly 630 CTT	TCA Ser	GAA Leu CTA	CAT Val 64	CAG Val 10 •	CCT Gly GAA	TTT Lys ATT	TGT Thr 550 GAA	TGT Thr	CAC Val	CTT Glu 660 GGA	TAA Ile AAA	TTT Lys	CTT Glu 67 AAA	CCA Gly>
CTT Glu • ACT TGA	Gly 630 GTT CAA	TCA Ser ACT TGA	GAA Leu CTA GAT	CAT Val 6	CAG Val 10 • AGA TCT	CCT Gly GAA CTT	TTT Lys ATT TAA	TGT Thr 550 GAA CTT	TGT Thr AAA TTT	CAC Val • GAT CTA	CTT Glu 660 GGA CCT	TAA Ile AAA TTT	TTT Lys • GTA CAT	CTT Glu 67 AAA TTT	CCA Gly> GTC CAG
CTT Glu • ACT TGA	Gly 630 GTT CAA	TCA Ser ACT TGA	GAA Leu CTA GAT	CAT Val 6	CAG Val 10 • AGA TCT	CCT Gly GAA CTT	TTT Lys ATT TAA	TGT Thr 550 GAA CTT	TGT Thr AAA TTT	CAC Val • GAT CTA	CTT Glu 660 GGA CCT	TAA Ile AAA TTT	TTT Lys • GTA CAT	CTT Glu 67 AAA TTT	CCA Gly>
CTT Glu • ACT TGA	GTT CAA Val	TCA Ser ACT TGA Thr	GAA Leu CTA GAT	CAT Val 6	CAG Val 10 * AGA TCT Arg	CCT Gly GAA CTT	TTT Lys ATT TAA	TGT Thr 550 GAA CTT Glu	TGT Thr AAA TTT Lys	CAC Val • GAT CTA	CTT Glu 660 GGA CCT Gly	TAA Ile AAA TTT Lys	TTT Lys • GTA CAT	CTT Glu 67 AAA TTT	CCA Gly> CC GTC CAG Val>
CTT Glu • ACT TGA	GTT CAA Val	TCA Ser ACT TGA	GAA Leu CTA GAT	CAT Val 6	CAG Val 10 • AGA TCT	CCT Gly GAA CTT	TTT Lys ATT TAA	TGT Thr 550 GAA CTT Glu	TGT Thr AAA TTT	CAC Val • GAT CTA	CTT Glu 660 GGA CCT Gly	TAA Ile AAA TTT	TTT Lys • GTA CAT	CTT Glu 67 AAA TTT	CCA Gly> GTC CAG
CTT Glu ACT TGA Thr	GTT CAA Val	TCA Ser ACT TGA Thr	GAA Leu CTA GAT Leu	CAT Val 64 AAA TTT Lys	CAG Val 10 AGA TCT Arg 690	CCT Gly GAA CTT Glu	TTT Lys ATT TAA Ile	TGT Thr 550 GAA CTT Glu	TGT Thr AAA TTT Lys	CAC Val GAT CTA Asp	CTT Glu 660 GGA CCT Gly	TAA Ile AAA TTT Lys	Lys GTA CAT Val	CTT Glu 67 AAA TTT Lys	CCA Gly> GTC CAG Val>
CTT Glu ACT TGA Thr	GTT CAA Val	TCA Ser ACT TGA Thr 680	GAA Leu CTA GAT Leu	CAT Val 64 AAA TTT Lys	CAG Val 10 AGA TCT Arg 690 GCA	CCT Gly GAA CTT Glu GGT	TTT Lys ATT TAA Ile TCT	TGT Thr 550 GAA CTT Glu 70	TGT Thr AAA TTT Lys	CAC Val GAT CTA ASP	CTT Glu 660 GGA CCT Gly	TAA Ile AAA TTT Lys	TTT Lys GTA CAT Val	CTT Glu 67 AAA TTT Lys	CCA Gly> GTC CAG Val> 720
CTT Glu ACT TGA Thr	GTT CAA Val	TCA Ser ACT TGA Thr 680 AAT TTA	GAA Leu CTA GAT Leu GAC CTG	CAT Val 64 AAA TTT Lys ACT TGA	CAG Val 10 AGA TCT Arg 690 GCA CGT	CCT Gly GAA CTT Glu GGT CCA	TTT Lys ATT TAA Ile TCT AGA	TGT Thr 550 GAA CTT Glu 70 AAC TTG	TGT Thr AAA TTT Lys 0 AAA TTT	CAC Val GAT CTA Asp	CTT Glu 660 GGA CCT Gly ACA TGT	AAA TTT Lys	TTT Lys GTA CAT Val AAA TTT	CTT Glu 67 AAA TTT Lys TGG ACC	CCA Gly> GTC CAG Val> 720 GAA CTT
CTT Glu ACT TGA Thr	GTT CAA Val	TCA Ser ACT TGA Thr 680 AAT TTA	GAA Leu CTA GAT Leu GAC CTG	CAT Val 64 AAA TTT Lys ACT TGA	CAG Val 10 AGA TCT Arg 690 GCA CGT	CCT Gly GAA CTT Glu GGT CCA	TTT Lys ATT TAA Ile TCT AGA	TGT Thr 550 GAA CTT Glu 70 AAC TTG	TGT Thr AAA TTT Lys 0 AAA TTT	CAC Val GAT CTA Asp	CTT Glu 660 GGA CCT Gly ACA TGT	AAA TTT Lys	TTT Lys GTA CAT Val AAA TTT	CTT Glu 67 AAA TTT Lys TGG ACC	CCA Gly> GTC CAG Val> 720
CTT Glu ACT TGA Thr	GTT CAA Val	ACT TGA Thr 680 AAT TTA ASD	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala	GAA CTT Glu GGT CCA Gly	TTT Lys ATT TAA Ile TCT AGA	TGT Thr 550 GAA CTT Glu 70 AAC TTG	TGT Thr AAA TTT Lys 00 AAA TTT Lys	CAC Val GAT CTA Asp	CTT Glu 660 GGA CCT Gly ACA TGT	AAA TTT Lys 10 GGT CCA Gly	TTT Lys GTA CAT Val AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC	CCA Gly> GTC CAG Val> 720 GAA CTT
CTT Glu ACT TGA Thr	GTT CAA Val	ACT TGA Thr 680 AAT TTA ASD	GAA Leu CTA GAT Leu GAC CTG	CAT Val 64 AAA TTT Lys ACT TGA	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala	CCT Gly GAA CTT Glu GGT CCA	TTT Lys ATT TAA Ile TCT AGA	TGT Thr 550 GAA CTT Glu 70 AAC TTG	TGT Thr AAA TTT Lys 0 AAA TTT	CAC Val GAT CTA Asp	CTT Glu 660 GGA CCT Gly ACA TGT	AAA TTT Lys	TTT Lys GTA CAT Val AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC	CCA Gly> GTC CAG Val> 720 GAA CTT
CTT Glu ACT TGA Thr TTT AAA Phe	GTT CAA Val	ACT TGA Thr 680 AAT TTA ASD	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala	GAA CTT Glu GGT CCA Gly	TTT Lys ATT TAA Ile TCT AGA Ser	TGT Thr 550 GAA CTT Glu 70 AAC TTG Asn	TGT Thr AAA TTT Lys AAA TTT Lys 750	CAC Val GAT CTA Asp AAA TTT Lys	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly	TTT Lys GTA CAT Val AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CC GTC CAG Val> 720 GAA CTT Glu>
CTT Glu ACT TGA Thr TTT AAA Phe	GTT CAA Val TTG AAC Leu	TCA Ser ACT TGA Thr 680 AAT TTA ASD 7	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala	GAA CTT Glu GGT CCA Gly	TTT Lys ATT TAA Ile TCT AGA Ser	TGT Thr 550 GAA CTT Glu 70 AAC TTG Asn	TGT Thr AAA TTT Lys 0 AAA TTT Lys 750	CAC Val GAT CTA Asp AAA TTT Lys	CTT Glu 660 GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76	TTT Lys GTA CAT Val AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> 720 CAA CTT Glu>
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG	GTT CAA Val TTG AAC Leu AGT TCA	ACT TGA Thr  680 AAT TTA ASD  ACT TGA	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT	GAA CTT Glu GGT CCA Gly 740 ACA TGT	TTT Lys ATT TAA Ile TCT AGA Ser ATT	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA	TGT Thr AAA TTT Lys O. AAA TTT Lys GCT CGA	CAC Val GAT CTA ASP AAA TTT Lys	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT	TTT Lys GTA CAT Val AAA TTT Lys GO	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> CAA CTT Glu> AAA TTT
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG	GTT CAA Val TTG AAC Leu AGT TCA	ACT TGA Thr  680 AAT TTA ASD  ACT TGA	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT	GAA CTT Glu GGT CCA Gly 740 ACA TGT	TTT Lys ATT TAA Ile TCT AGA Ser ATT	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA	TGT Thr AAA TTT Lys O. AAA TTT Lys GCT CGA	CAC Val GAT CTA ASP AAA TTT Lys	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT	TTT Lys GTA CAT Val AAA TTT Lys GO	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> CAA CTT Glu> AAA TTT
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG	GTT CAA Val TTG AAC Leu AGT TCA	ACT TGA Thr  680 AAT TTA ASD  ACT TGA	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT	GAA CTT Glu GGT CCA Gly 740 ACA TGT	TTT Lys ATT TAA Ile TCT AGA Ser ATT	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA	TGT Thr AAA TTT Lys O. AAA TTT Lys GCT CGA	CAC Val GAT CTA ASP AAA TTT Lys	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT	TTT Lys GTA CAT Val AAA TTT Lys GO	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> 720 CAA CTT Glu>
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG	GTT CAA Val TTG AAC Leu AGT TCA	ACT TGA Thr  680 AAT TTA ASD  ACT TGA	GAA Leu CTA GAT Leu GAC CTG Asp	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT	GAA CTT Glu GGT CCA Gly 740 ACA TGT	TTT Lys ATT TAA Ile TCT AGA Ser ATT	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA	AAA TTT Lys O. AAA TTT Lys 750 GCT CGA Ala	CAC Val GAT CTA ASP AAA TTT Lys	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT	TTT Lys GTA CAT Val AAA TTT Lys GO	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> CAA CTT Glu> AAA TTT
CTT Glu ACT TGA Thr TTT AAA Phe GAC CTG Asp	GTT CAA Val TTG AAC Leu AGT TCA	ACT TGA Thr  680 AAT TTA ASD  ACT TGA	GAA Leu CTA GAT Leu GAC CTG Asp 30 * AGC TCG Ser	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT	GAA CTT Glu GGT CCA Gly 740 ACA TGT	TTT Lys ATT TAA Ile TCT AGA Ser ATT TAA Ile	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA	AAA TTT Lys O. AAA TTT Lys 750 GCT CGA Ala	CAC Val GAT CTA ASP AAA TTT Lys GAC CTG ASP	GGA CCT Gly ACA TGT Thr	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT	CTA CAT Val  AAA TTT Lys AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC TTP	CCA Gly> CTC CAG Val> CAA CTT Glu> AAA TTT
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG ASP	GTT CAA Val  TTG AAC Leu  AGT TCA Ser	ACT TGA AST TGA AST TGA Thr	GAA Leu CTA GAT Leu GAC CTG Asp 30 * AGC TCG Ser 780	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT Leu	GAA CTT Glu GGT CCA Gly 740 ACA TGT Thr	TTT Lys ATT TAA Ile TCT AGA Ser ATT TAA Ile	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA Ser	AAA TTT Lys 750 GCT CGA Ala	GAT CTA ASP AAA TTT Lys GAC CTG ASP	GGA CCT Gly ACA TGT Thr AGC TCG Ser	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT Lys	CTA CAT Val AAA TTT Lys AAA TTT Lys	CTT Glu 67 AAA TTT Lys TGG ACC Trp ACT TGA Thr	CCA Gly> CTC CAG Val> 720 CAA CTT Glu> AAA TTT Lys>
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG Asp 770 GAT	GTT CAA Val  TTG AAC Leu  AGT TCA Ser	TCA Ser ACT TGA Thr 680 AAT TTA ASD ACT TGA Thr	GAA Leu CTA GAT Leu GAC CTG Asp 30 * AGC TCG Ser 780 * TTC	CAT Val 64 AAA TTT Lys ACT TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT Leu	GAA CTT Glu GGT CCA Gly 740 ACA TGT Thr	TTT Lys ATT TAA Ile TCT AGA Ser ATT TAA Ile	TGT Thr 50 GAA CTT Glu 70 AAC TTG ASN AGT TCA Ser	TGT Thr AAA TTT Lys 750 GCT CGA Ala	GAT CTA ASP AAA TTT Lys GAC CTG ASP B00 ACA	GGA CCT Gly ACA TGT Thr AGC TCG Ser	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT Lys	TIT Lys GTA CAT Val AAA TTT Lys 810 CAA	CTT Glu 67 AAA TTT Lys TGG ACC TTP ACT TGA Thr	CCA Gly> CTC CAG Val> 720 CAA CTT Glu> AAA TTT Lys>
CTT Glu  ACT TGA Thr  TTT AAA Phe GAC CTG Asp 770 GAT CTA	GTT CAA Val TTG AAC Leu TTG AAC TTG AAC	ACT TGA THE TTA ASD THE TGA TGA THE TG	GAA Leu CTA GAT Leu GAC CTG ASP 30 * AGC TCG Ser 780 * TTC AAG	CAT Val 64 AAA TTT Lys ACT TGA Thr TGA Thr	CAG Val 10 AGA TCT Arg 690 GCA CGT Ala TTA AAT Leu	GAA CTT Glu GGT CCA Gly ACA TGT Thr	TTT Lys ATT TAA Ile TCT AGA Ser ATT TAA Ile GGT CCA	TGT Thr 550 GAA CTT Glu 70 AAC TTG ASD AGT TCA Ser	TGT Thr AAA TTT Lys 750 GCT CGA Ala ATT	GAT CTA ASP AAA TTT Lys GAC CTG ASP BOO ACA TGT	GGA CCT Gly ACA TGT Thr AGC TCG Ser	AAA TTT Lys 10 GGT CCA Gly 76 AAA TTT Lys	CAA GTA CAT Val  AAA TTT Lys 810 CAA GTT	CTT Glu 67 AAA TTT Lys TGG ACC Trp ACT TGA Thr	CCA Gly> CTC CAG Val> 720 CAA CTT Glu> AAA TTT Lys>

820 830 840 850 860

ACA GCT GGA ACC AGC CTA GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT
TGT CGA CCT TGG TCG GAT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA
Thr Ala Gly Thr Ser Leu Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu>

870 880 890

\*\*

TCA GAG CTT AAA AAC GCT TTA AAA TAA
AGT CTC GAA TTT TTG CGA AAT TTT ATT
Ser Glu Leu Lys Asn Ala Leu Lys \*\*\*>

FIGURE 11 (3 of 3)

OspC-B31 Sequence Range: 1 to 633

10	20	•	30	40
•	• •	•	•.	•
ATG AAA AAG AAT A	ACA TTA AG	T GCG ATA T	TA ATG ACT T	TIT ATT TIT ATT
TAC TIT TIC TIA	rgt aat tc	A CGC TAT A	AT TAC TGA A	AAA TAA AAA TAA
Met Lys Lys Asn	Thr Leu Se	r Ala Ile L	eu Met Thr I	Leu Phe Leu Phe>
	•		00	00
50 60	•	70	80	90
ATA TOT TGT AAT	*	ር እአአ ርአጥ ር	י רב אגיד ארא יו	יייי כרא אאיז יייייי
TAT AGA ACA TTA	RAT ICA GG	C TOTO COLL C	CC TTA TGT A	AGA OGT TTA AGA
Ile Ser Cys Asn	Asn Ser Gl	v Lvs Asp G	lv Asn Thr S	Ser Ala Asn Ser>
Tie ser cha usu :		,,, .	<b>-</b>	
100 1	10 -	120	130	140
* *	* *	•	* *	• •
GCT GAT GAG TCT	GTT AAA GG	G CCT AAT C	TT ACA GAA A	ATA AGT AAA AAA
CGA CTA CTC AGA	CAA TIT CC	C GGA TTA G	AA TGT CTT	PAT TCA TIT TIT .
Ala Asp Glu Ser	Val Lys Gl	y Pro Asn L	eu Thr Glu	Ile Ser Lys Lys>
			• • • •	•••
150	160	170	180	190
ATT ACG GAT TCT	*	AD WAR CALL C	·~•	ראר רייי ראז רריי
TAA TGC CTA AGA				
Ile Thr Asp Ser	lin coc ca	d Lev Lev A	la Val Lvs (	Glu Val Glu Ala>
Tie IIII wah ser	ASII ALU VU	200 200		
200	210	220	2:	30 240
• •	* *	* *	• •	• •
TTG CTG TCA TCT				
AAC GAC AGT AGA				
Leu Leu Ser Ser	Ile Asp Gl	lu Ile Ala A	ala Lys Ala	Ile Gly Lys Lys>
250	260	, ,	270	280
250	* *		* *	200 * *
ATA CAC CAA AAT	AAT GGT TT	TG GAT ACC G	SAA TAT AAT	CAC AAT GGA TCA
			ATT ATA TTA	GTG TTA CCT AGT
Ile His Gln Asn				•
			Slu Tyr Asn	•
				•
Ile His Gln Asn 290 300	Asn Gly Le	310	320	His Asn Gly Ser>
Ile His Gln Asn 290 300 TTG TTA GCG GGA	Asn Gly Le	310 CA ATA TCA A	320 ACC CTA ATA	His Asn Gly Ser> 330 AAA CAA AAA TTA
Ile His Gln Asn 290 300 * * * TTG TTA GCG GGA AAC AAT CGC CCT	Asn Gly Le  CGT TAT GG GCA ATA CG	310 * CA ATA TCA I	320 * ACC CTA ATA IGG GAT TAT	His Asn Gly Ser> 330 AAA CAA AAA TTA TTT GTT TTT AAT
Ile His Gln Asn 290 300 * * * TTG TTA GCG GGA AAC AAT CGC CCT	Asn Gly Le  CGT TAT GG GCA ATA CG	310 * CA ATA TCA I	320 *ACC CTA ATA IGG GAT TAT	His Asn Gly Ser> 330 AAA CAA AAA TTA
Ile His Gln Asn 290 300 TTG TTA GCG GGA AAC AAT CGC CCT Leu Leu Ala Gly	Asn Gly Le  CGT TAT GG GCA ATA CG	310 * CA ATA TCA I	320 *ACC CTA ATA IGG GAT TAT	His Asn Gly Ser> 330 AAA CAA AAA TTA TTT GTT TTT AAT
Ile His Gln Asn 290 300 TTG TTA GCG GGA AAC AAT CGC CCT Leu Leu Ala Gly	CGT TAT GG GCA ATA CG Arg Tyr A	310 CA ATA TCA A GT TAT AGT S	320 ACC CTA ATA IGG GAT TAT Thr Leu Ile	His Asn Gly Ser> 330 AAA CAA AAA TTA TTT GTT TTT AAT Lys Gln Lys Leu>
Ile His Gln Asn 290 300 TTG TTA GCG GGA AAC AAT CGC CCT Leu Leu Ala Gly 340 GAT GGA TTG AAA	CGT TAT GG GCA ATA CG Arg Tyr A	SU ASP Thr G 310 CA ATA TCA A GT TAT AGT S 1a Ile Ser S 360 GA TTA AAG	320 ACC CTA ATA IGG GAT TAT Thr Leu Ile 370 GAA AAA ATT	His Asn Gly Ser>  330  AAA CAA AAA TTA TTT GTT TTT AAT Lys Gln Lys Leu>  380  GAT GCG GCT AAG
Ile His Gln Asn  290 300  TTG TTA GCG GGA AAC AAT CGC CCT Leu Leu Ala Gly  340  GAT GGA TTG AAA CTA CCT AAC TTT	CGT TAT GG GCA ATA CG Arg Tyr A: 350 AAT GAA GG TTA CTT C	SU ASP Thr G 310 CA ATA TCA A GT TAT AGT S 1a Ile Ser S 360 GA TTA AAG G CT AAT TTC	320 ACC CTA ATA IGG GAT TAT Thr Leu Ile 370 GAA AAA ATT CTT TTT TAA	His Asn Gly Ser> 330 AAA CAA AAA TTA TTT GTT TTT AAT Lys Gln Lys Leu> 380

FIGURE 12 (1 of 2)

OspC-B31

420 390 AAA TGT TCT GAA ACA JTT ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT TTT ACA AGA CTT TGT AAA TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA Lys Cys Ser Glu Thr Phe Thr Asn Lys Leu Lys Glu Lys His Thr Asp> 470 4'50 460 480 CTT GGT AAA GAA GGT GTT ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA GAA CCA TTT CTT CCA CAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT Leu Gly Lys Glu Gly Val Thr Asp Ala Asp Ala Lys Glu Ala Ile Leu> 510 -490 500 AAA ACA AAT GGT ACT AAA ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TIT TGT TTA CCA TGA TTT TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT Lys Thr Asn Gly Thr Lys Thr Lys Gly Ala Glu Glu Leu Gly Lys Leu> 530 540 550 560 TTT GAA TCA GTA GAG GTC TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAA CTT AGT CAT CTC CAG AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA Phe Glu Ser Val Glu Val Leu Ser Lys Ala Ala Lys Glu Met Leu Ala> 590 600 610 580 620 AAT TCA GTT AAA GAG CTT ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA TTA AGT CAA TTT CTC GAA TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT Asn Ser Val Lys Glu Leu Thr Ser Pro Val Val Ala Glu Ser Pro Lys> 630 AAA CCT TAA TTT GGA ATT Lys Pro \*\*\*>

FIGURE 12 (2 of 2)

OspC-K48
Sequence Range: 1 to 630

22/133

20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TIT TIC TIA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 50 60 70 80 ATA TCT TGT AAT AAT TCA GGT GGG GAT ACC GCA TCT ACT AAT CCT GAT TAT AGA ACA TTA TTA AGT CCA CCC CTA TGG CGT AGA TGA TTA GGA CTA Ile Ser Cys Asn Asn Ser Gly Gly Asp Thr Ala Ser Thr Asn Pro Asp> 110 120 GAG TCT GCA AAA GGA CCT AAT CTT ACA GTA ATA AGC AAA AAA ATT ACA CTC AGA CGT TTT CCT GGA TTA GAA TGT CAT TAT TCG TTT TTT TAA TGT Glu Ser Ala Lys Gly Pro Asn Leu Thr Val Ile Ser Lys Lys Ile Thr> 160 170 180 190 GAT TCT AAT GCA TTT GTA CTG GCT GTG AAA GAA GTT GAG GCT TTG ATC CTA AGA TTA CGT AAA CAT GAC CGA CAC TTT CTT CAA CTC CGA AAC TAG Asp Ser Asn Ala Phe Val Leu Ala Val Lys Glu Val Glu Ala Leu Ile> 220 230 240 TCA TCT ATA GAT GAA CTT GCT AAT AAA GCT ATT GGT AAA GTA ATA CAT AGT AGA TAT CTA CTT GAA CGA TTA TTT CGA TAA CCA TTT CAT TAT GTA Ser Ser Ile Asp Glu Leu Ala Asn Lys Ala Ile Gly Lys Val Ile His> ~ 250 260 270 CAA AAT AAT GGT TTA AAT GCT AAT GCG GGT CAA AAC GGA TCA TTG TTA GTT TTA TTA CCA AAT TTA CGA TTA CGC CCA GTT TTG CCT AGT AAC AAT Gln Asn Asn Gly Leu Asn Ala Asn Ala Gly Gln Asn Gly Ser Leu Leu> 290 300 310 GCA GGA GCC TAT GCA ATA TCA ACC CTA ATA ACA GAA AAA TTA AGT AAA CGT CCT CGG ATA CGT TAT AGT TGG GAT TAT TGT CTT TTT AAT TCA TTT Ala Gly Ala Tyr Ala Ile Ser Thr Leu Ile Thr Glu Lys Leu Ser Lys> 350 360 370 TTG AAA AAT TCA GAA GAG TTA AAT AAA AAA ATT GAA GAG GCT AAG AAC AAC TIT TTA AGT CIT CTC AAT TTA TIT TAA CIT CTC CGA TIC TIG Leu Lys Asn Ser Glu Glu Leu Asn Lys Lys Ile Glu Glu Ala Lys Asn>

FIGURE 13 (1 of 2)

OBDC-K48

390 400 CAT TCT GAA GCA TTT ACT AAT AGA CTA AAA GGT TCT CAT GCA CAA CTT GTA AGA CTT CGT AAA TGA TTA TCT GAT TTT CCA AGA GTA CGT GTT GAA His Ser Glu Ala Phe Thr Asn Arg Leu Lys Gly Ser His Ala Gln Leu> 450 460 470 GGA GTT GCT GCT ACT GAT GAT CAT GCA AAA GAA GCT ATT TTA AAG CCT CAA CGA CGA TGA CTA CTA GTA CGT TTT CTT CGA TAA AAT TTC Gly Val Ala Ala Thr Asp Asp His Ala Lys Glu Ala Ile Leu Lys> 490 500 510 T, ===== • TCA AAT CCT ACT AAA GAT AAG GGT GCT AAA GCA CTT AAA GAC TTA TCT AGT TTA GGA TGA TTT CTA TTC CCA CGA TTT CGT GAA TTT CTG AAT AGA Ser Asn Pro Thr Lys Asp Lys Gly Ala Lys Ala Leu Lys Asp Leu Ser> 530 540 550 560 570 GAA TCA GTA GAA AGC TTG GCA AAA GCA GCG CAA GAA GCA TTA GCT AAT CTT AGT CAT CTT TCG AAC CGT TTT CGT CGC GTT CTT CGT AAT CGA TTA Glu Ser Val Glu Ser Leu Ala Lys Ala Ala Gln Glu Ala Leu Ala Asn> 590 600 610 620 TCA GTT AAA GAA CTT ACA AAT CCT GTT GTG GCA GAA AGT CCA AAA AAA AGT CAA TTT CTT GAA TGT TTA GGA CAA CAC CGT CTT TCA GGT TTT TTT Ser Val Lys Glu Leu Thr Asn Pro Val Val Ala Glu Ser Pro Lys Lys> 630 CCT TAA GGA ATT Pro \*\*\*>

FIGURE 13 (2 of 2)

OspC-PKO Sequence Range: 1 to 639

20 ATG AAA AAG AAT ACA TTA AGT GCG ATA TTA ATG ACT TTA TTT TTA TTT TAC TTT TTC TTA TGT AAT TCA CGC TAT AAT TAC TGA AAT AAA AAT AAA Met Lys Lys Asn Thr Leu Ser Ala Ile Leu Met Thr Leu Phe Leu Phe> 50 60 80 ATA TOT TGT AGT AAT TOA GGG AAA GGT GGG GAT TOT GCA TOT ACT AAT TAT AGA ACA TCA TTA AGT CCC TTT CCA CCC CTA AGA CGT AGA TGA TTA Ile Ser Cys Ser Asn Ser Gly Lys Gly Gly Asp Ser Ala Ser Thr Asn> 100 110 120 130 CCT GCT GAC GAG TCT GCG AAA GGG CCT AAT CTT ACA GAA ATA AGC AAA GGA CGA CTG CTC AGA CGC TTT CCC GGA TTA GAA TGT CTT TAT TCG TTT Pro Ala Asp Glu Ser Ala Lys Gly Pro Asn Leu Thr Glu Ile Ser Lys> 150 160 170 180 AAA ATT ACA GAT TCT AAT GCA TTT GTA CTT GCT GTT AAA GAA GTT GAG TTT TAA TGT CTA AGA TTA CGT AAA CAT GAA CGA CAA TTT CTT CAA CTC Lys Ile Thr Asp Ser Asn Ala Phe Val Leu Ala Val Lys Glu Val Glu> 200 210 220 240 ACT TTG GTT TTA TCT ATA GAT GAA CTT GCT AAG AAA GCT ATT GGT CAA TGA AAC CAA AAT AGA TAT CTA CTT GAA CGA TTC TTT CGA TAA CCA GTT Thr Leu Val Leu Ser Ile Asp Glu Leu Ala Lys Lys Ala Ile Gly Gln> 260 270 AAA ATA GAC AAT AAT AAT GGT TTA GCT GCT TTA AAT AAT CAG AAT GGA TTT TAT CTG TTA TTA TTA CCA AAT CGA CGA AAT TTA TTA GTC TTA CCT-Lys Ile Asp Asn Asn Gly Leu Ala Ala Leu Asn Asn Gln Asn Gly> 290 300 310 320 330 TCG TTG TTA GCA GGA GCC TAT GCA ATA TCA ACC CTA ATA ACA GAA AAA AGC AAC AAT CGT CCT CGG ATA CGT TAT AGT TGG GAT TAT TGT CTT TTT Ser Leu Leu Ala Gly Ala Tyr Ala Ile Ser Thr Leu Ile Thr Glu Lys> 340 350 360 370. 380 TTG AGT AAA TTG AAA AAT TTA GAA GAA TTA AAG ACA GAA ATT GCA AAG AAC TCA TTT AAC TTT TTA AAT CTT CTT AAT TTC TGT CTT TAA CGT TTC Leu Ser Lys Leu Lys Asn Leu Glu Glu Leu Lys Thr Glu Ile Ala Lys>

### OspC-PKO

	390			40	00		4	10			420			43	30
•	*		•		•	•		•		•	•		•		•
CCT	AAG	AAA	TGT	TCC	GAA	GAA	TTT	ACT	TAA	AAA	CTA	AAA	AGT	GGT	CAT
CGA	TTC	TTT	ACA	AGG	CTT	CTT	AAA	TGA	TTA	TTT	GAT	TTT	TCA	CCA	GTA
λla	LVS	LVS	CVS	Ser	Glu	Glu	Phe	Thr	Asn	Lys	Leu	Lys	Ser	Gly	His>
7,10	<b>J</b>	_,_	-, -											_	
	4	140			450			46	50		4	170			480
•		•		•	•		•		•	. •		•		•	•
GCA	GAT	CTT	GGC	AAA	CAG	GAT	GCT	ACC	GAT	GAT	CAT	GCA	AAA	GCA	GCT
CGT	CTA	GAA	CCG	TTT	GTC	CTA	CGA	TGG	CTA	CTA	GTA	CGT	TTT	CGT	CGA
Ala	Asp	Leu	Gly	Lys	Gln	Asp	Ala	Thr	Asp	Asp	His	Ala	Lys	Ala	Ala>
	_									_					
		45	90		5	500			510		•	52	20		•
	•		•	*		#		•	•		•		•	•	
					GCA										
TAA	AAT	TTT	TGT	GTA	CGT	TGA	TGG	CTA	TTT	CCA	CGA	TTT	CII	AAA	TTT
Ile	Leu	Lys	Thr	His	Ala	Thr	Thr	λsp	Lys	Gly	Ala	Lys	Glu	Phe	Lys>
4套															
530			540			5	50			560			570		
•		•	•		*		*	•		*		•	*		•
GAT	TTA	TTT	GAA	TCA	GTA	GAA	GGT	TTG	TTA	AAA	GCA	CCT	CAA	GTA	GCA
CTA	<b>TAA</b>	AAA	CTT	AGT	CAT	CII	CCA	AAC	AAT	TIT	CGT	CGA	GTT	CAT	CGT
Asp	Leu	Phe	Glu	Ser	Val	Glu	Gly	Leu	Leu	Lys	Ala	Ala	Gln	Val	Ala>
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5	80	٠.		590			600		•	0.	10 .		,	520	
	*					~	~~~	101	> CT			~~~	CC1	~ .	<b>&gt;</b> C C C
	ACT				AAA.										
~ ~ ~ ~			- ~~	~	~~~										
	TGA														
															Ser>
	Thr														
Leu	Thr 630	, Asn	`Ser	Val.	_Lys										
Leu	Thr 630	Asn AAA	Ser	Val.	_Lys										
Leu CCA GGT	Thr 630 AAA TTT	AAA TTT	Ser CCT GGA	Val.	Lys										

FIGURE 14 (2 of 2)

OspC-TRO

Sequence Range: 1 to 624

			10			20			30		_		40		
ATG	AAA	AAG	AAT	ACA	TTA	AGT	GCG	ATA	ATT	STG.	<b>y</b>	ጥተል	.detet.	الانت 4 -	TTT
TAC	TIT	TTC	TTA	TGT	AAT	TCA	CGC	TAT	AAT	TAC	TGA	AAT	AAA	TIM TAK	AAA
Met	Lys	Lys	Asn	Thr	Leu	Ser	Ala	Ile	Leu	Met	Thr	Leu	Phe	Leu	Phe>
													•		
50 •		•	60		•		70	•		80			90		
ATA	TCT	TGT	AAT	TAA	TCA	GGT	GGG	GAT	тст	GCA	<b>T</b> (T	ACT.	አ አጥ	CC41	GAT
TAT	AGA	ACA	TTA	TTA	AGT	CCA	CCC	CTA	AGA	CGT	AGA	TGA	TTA	GGA	CTA
Ile	Ser	Cys	Asn	Asn	Ser	Gly	Gly	Asp	Ser	Ala	Ser	Thr	Asn	Pro	Asp>
															-
10	00		•	110		٠.	120			1.	30	٠		140	• -
GAG	TCT	GCA	AAA	GGA	CCT	AAT	CTT	ACC	GTA	АТА	ycc.	444	222	y ava	202
CTC	AGA	CGT	TTT	CCT	GGA	TTA	GAA	TGG	CAT	TAT	TCG	TTT	TTT	TAA	TGT
Glu	Ser	Ala	Lys	Gly	Pro	Asn	Leu	Thr	Val	Ile	Ser	Lys	Lys	Ile	Thr>
						•			٠						
•	150		*	16	*	*	•	170			180		_	19	90
GAT	TCT	TAA	GCA	TTT	TTA	CTG	GCT	GTG	AAA	GAA	CTT	GAG	CCT.	17TC	CTT
CTA	AGA	TTA	CGT	AAA	TAA	GAC	CGA	CAC	TIT	CTT	CAA	CTC	CGA	AAC	GAA
λsp	Ser	Asn	Ala	Phe	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala	Leu	Leu>
		200			210			~-							_
•	4	•		•	210		•	22	*	•	4	30			240
TCA	TCT	ATA	GAT	GAA	CTT	TCT	AAA	GCT	ATT	GGT	AAA	λλλ	ATA	AAA	AAT
AGT	AGA	TAT	CTA	CTT	GAA	AGA	TTT	CGA	TAA	CCA	TTT	TTT	TAT	TTT	TTA
Ser	Ser	Ile	Asp	Glu	Leu	Ser	Lys	Ala	Ile	Gly	Lys	Lys	Ile	Lys	Asn>
		25	50		2	260			270			28	20		•
	•		•	•		'♠		•	•		•		•	•	
GAT	GGT	ACT	TTA	GAT	AAC	GAA	GCA	AAT	CGA	AAC	GAA	TCA	تكلحك	ATA	GCA
ACD	CCI										<b></b>		110		
rap	Clu	TGA	AAT	CTA	TTG	CII	CGT	TTA	GCT	TTG	CTT	AGT	AAC	TAT	CGT
_	Gly	Thr	AAT Leu	CTA	TTG	CII	CGT	TTA	GCT	TTG	CTT	AGT	AAC	TAT	CGT Ala>
290	Gly	Thr	AAT Leu 300	CTA	TTG	CII	CGT	TTA	GCT Arg	TTG	CTT	AGT	AAC Leu	TAT	CGT Ala>
290	Gly	Thr	300	CTA Asp	TTG Asn	Glu 31	CGT Ala	TTA Asn	GCT Arg	TTG Asn 20	CIT Glu	AGT Ser	AAC Leu 330	TAT Ile	CGT Ala>
290 ± GGA	Gly	Thr • TAT	JOU GAA	CTA Asp	TTG Asn • TCA	Glu 31	CGT Ala 10 *	TTA Asn • ATA	GCT Arg	TTG Asn 20	CTT Glu AAA	AGT Ser	AAC Leu 330	TAT Ile	Ala>
290 * GGA CCT	Gly GCT CGA	Thr TAT ATA	Jeu 300 GAA CTT	CTA Asp ATA TAT	TTG Asn • TCA AGT	Glu 31 AAA TTT	CGT Ala 10 * CTA GAT	TTA Asn • ATA TAT	GCT Arg 3 ACA TGT	TTG Asn 20 CAA GTT	CTT Glu AAA TTT	AGT Ser * TTA AAT	AAC Leu 330 + AGT TCA	TAT Ile GTA CAT	Ala> TTG
290 * GGA CCT	Gly GCT CGA	Thr TAT ATA	Jeu 300 GAA CTT	CTA Asp ATA TAT	TTG Asn • TCA AGT	Glu 31 AAA TTT	CGT Ala 10 * CTA GAT	TTA Asn • ATA TAT	GCT Arg 3 ACA TGT	TTG Asn 20 CAA GTT	CTT Glu AAA TTT	AGT Ser * TTA AAT	AAC Leu 330 + AGT TCA	TAT Ile GTA CAT	Ala>
290 GGA CCT Gly	Gly GCT CGA	Thr TAT ATA	GAA CTT Glu	CTA Asp ATA TAT	TTG Asn • TCA AGT	Glu 31 AAA TTT	CGT Ala 10 * CTA GAT	TTA Asn • ATA TAT	GCT Arg 3 ACA TGT	TTG Asn 20 CAA GTT	CTT Glu AAA TTT Lys	AGT Ser * TTA AAT	AAC Leu 330 * AGT TCA Ser	TAT Ile GTA CAT	Ala> TTG
290 GGA CCT Gly	GCT CGA Ala	Thr TAT ATA Tyr	GAA CTT Glu	ATA TAT Ile	TTG Asn TCA AGT Ser	Glu 31 AAA TTT Lys	CGT Ala 10 * CTA GAT Leu 360	ATA TAT Ile	GCT Arg ACA TGT Thr	CAA GTT Gln	CTT Glu AAA TTT Lys	AGT Ser * TTA AAT Leu	AAC Leu 330 * AGT TCA Ser	TAT Ile GTA CAT Val 80 *	Ala> TTG AAC Leu>
290 GGA CCT Gly 34	GCT CGA Ala	Thr TAT ATA Tyr	GAA GAA GAA	ATA TAT Ile	TTG Asn TCA AGT Ser	Glu 31 AAA TTT Lys AAA	CGT Ala 10 * CTA GAT Leu 360 *	ATA TAT Ile	GCT Arg ACA TGT Thr	TTG Asn 20 CAA GTT Gln 37	CTT Glu AAA TTT Lys 0	AGT Ser * TTA AAT Leu AAG	AAC Leu 330 AGT TCA Ser	TAT Ile GTA CAT Val 80 + TGT	Ala> TTG AAC Leu>
GGA CCT Gly 34 AAT TTA	GIY GCT CGA Ala 10 TCA AGT	Thr TAT ATA Tyr GAA CTT	GAA CTT GAA CTT	ATA TAT Ile	TTG Asn TCA AGT Ser AAG TTC	Glu 31 AAA TTT Lys AAA TTT	CGT Ala 10 * CTA GAT Leu 360 * AAA	ATA TAT Ile	GCT Arg ACA TGT Thr AAA TTT	TTG Asn 20 CAA GTT Gln 37 GAG CTC	AAA TTT Lys GCT CGA	AGT Ser TTA AAT Leu AAG TTC	AAC Leu 330 * AGT TCA Ser 3 GAT CTA	TAT Ile GTA CAT Val 80 + TGT	Ala> TTG AAC Leu>

OSDC-TRO

	390			40	00		4	110			420			4	30
•	•	•	*		•	•		•		•	•		. •		•
GAA	AAA	TTT	ACT	ACT	AAG	CTA	AAA	GAT	AGT	CAT	GCA	GAG	CTT	GGT	ATA
CTT	TTT	AAA	TGA	TGA	TTC	GAT	TTT	CTA	TCA	GTA	CGT	CTC	GAA	CCA	TAT
Glu	Lys	Phe	Thr	Thr	Lys	Leu	Lys	Asp	Ser	His	Ala	Glu	Leu	Gly	Ile>
	•	•													
	4	40		•	450			46	50		4	170			480
•		•		*	•		• •		•	•		•		•	•
CAA	AGC	GTT	CAG	GAT	GAT	AAT	GCA	AAA	AAA	GCT	ATT	TTA	AAA	ACA	CAT
GTT	TCG	CAA	GTC	CTA	CTA	TTA	CGT	TTT	TTT	CGA	TAA	AAT	TTT	TGT	GTA
															His>
				-	_		•		-				Ū		
		45	90		9	500			510		··· ··	52	20		٠.
	*		*	*		•		*	•		•		•	•	
GGA	ACT	AAA	GAC	AAG	GGT	GCT	AAA	GAA	CTT	GAA	GAG	TTA	TTT	AAA	TCA
															AGT
															Ser>
3		•	•	-	_								-	-	
530	•		540			55	50	•	9	560			570		
•		•	•		•		•	•		•		• .	•		•
CTA	GAA	AGC	TTG	TCA	AAA	GCA	GCG	CAA	GCA	GCA	TTA	ACT	AAT	TCA	GII
GAT	CTT	TCG	AAC	AGT	TTT	CGT	CGC	GTT	CGT	CGT	TAA	TGA	TTA	AGT	CAA ·
Leu	Glu	Ser	Leu	Ser	Lys	Ala	Ala	Gln	Ala	Ala	Leu	Thr	Asn	Ser	Val>
			•			*									
58	80		:	590			600			61	LO		6	520	
	*	•		•		•	*		•		•	•		<b>*</b> ,	
AAA	GAG	CTT	ACA	AAT	CCT	GTT	GTG	GCA	GAA	AGT	CCA	AAA	AAA	CCT	TAA
TIT	CTC	GAA	TGT	TTA	GGA	CAA	CAC	CGT	CTT	TCA	GGT	TTT	TIT	GGA	TTA
Lys	Glu	Leu	Thr	Asn	Pro	Val	Val	Ala	Glu	Ser	Pro	Lys	Lys	Pro	***>

FIGURE 15 (2 of 2)

P93

Sequence Range: 1 to 2102

30 ATG AAA AAA ATG TTA CTA ATC TTT AGT TTT TTT CTT ATT TTC TTG AAT TAC TIT TIT TAC AAT GAT TAG AAA TCA AAA AAA GAA TAA AAG AAC TTA Met Lys Lys Met Leu Leu Ile Phe Ser Phe Phe Leu Ile Phe Leu Asn> 80 60 70 50 GGA TIT CCT GTT AGT GCA AGA GAA GTT GAT AGG GAA AAA TTA AAG GAC CCT AAA GGA CAA TCA CGT TCT CTT CAA CTA TGG-CTT TTT AAT TTC CTG Gly Phe Pro Val Ser Ala Arg Glu Val Asp Arg Glu Lys Leu Lys Asp> - 120 130 110 100 TTT GTT AAT ATG GAT CTT GAG TTT GTA AAT TAT AAA GGC CCT TAT GAT AAA CAA TTA TAC CTA GAA CTC . A CAT TTA ATA TTT CCG GGA ATA CTA Phe Val Asn Met Asp Leu Glu Phe Val Asn Tyr Lys Gly Pro Tyr Asp> 170 180 160 TCT ACA AAT ACA TAT GAA CAA ATA GTG GGT ATT GGG GAG TTT TTA GCA AGA TGT TTA TGT ATA CTT GTT TAT CAC CCA TAA CCC CTC AAA AAT CGT Ser Thr Asn Thr Tyr Glu Gln Ile Val Gly Ile Gly Glu Phe Leu Ala> 220 230 240 200 AGA CCG TTG ACC AAT TCC AAT AGC AAC TCA AGT TAT TAT GGT AAA TAT TCT GGC AAC TGG TTA AGG TTA TCG TTG AGT TCA ATA ATA CCA TTT ATA Arg Pro Leu Thr Asn Ser Asn Ser Asn Ser Ser Tyr Tyr Gly Lys Tyr> 270 280 250 TTT ATT AAT AGA TTT ATT GAT GAT CAA GAT AAA AAA GCA AGC GTT GAT AAA TAA TTA TCT AAA TAA CTA CTA GTT CTA TTT TTT CGT TCG CAA CTA Phe Ile Asn Arg Phe Ile Asp Asp Gln Asp Lys Lys Ala Ser Val Asp> 330 320 300 310 290 GTT TTT TCT ATT GGT AGT AAG TCA GAG CTT GAC AGT ATA TTG AAT TTA CAA AAA AGA TAA CCA TCA TTC AGT CTC GAA CTG TCA TAT AAC TTA AAT Val Phe Ser Ile Gly Ser Lys Ser Glu Leu Asp Ser Ile Leu Asn Leu> 360 370 380 340 350 AGA AGA ATT CTT ACA GGG TAT TTA ATA AAG TCT TTC GAT TAT GAC AGG TCT TCT TAA GAA TGT CCC ATA AAT TAT TTC AGA AAG CTA ATA CTG TCC Arg Arg Ile Leu Thr Gly Tyr Leu Ile Lys Ser Phe Asp Tyr Asp Arg>

FIGURE 16 (1 of 5)

390 400 420 TCT AGT GCA GAA TTA ATT GCT AAG GTT ATT ACA ATA TAT AAT GCT GTT AGA TCA CGT CTT AAT TAA CGA TTC CAA TAA TGT TAT ATA TTA CGA CAA Ser Ser Ala Glu Leu Ile Ala Lys Val Ile Thr Ile Tyr Asn Ala Val> 440 450 460 470 TAT AGA GGA GAT TTG GAT TAT TAT AAA GGG TTT TAT ATT GAG GCT GCT ATA TCT CCT CTA AAC CTA ATA ATA TTT CCC AAA ATA TAA CTC CGA CGA Tyr Arg Gly Asp Leu Asp Tyr Tyr Lys Gly Phe Tyr Ile Glu Ala Ala> 500 510 . . = . . . TTA AAG TCT TTA AGT AAA GAA AAT GCA GGT CTT TCT AGG GTT TAT AGT ART TTC AGA ART TCA TTT CTT TTA CGT CCA GAA AGA TCC CAA ATA TCA Leu Lys Ser Leu Ser Lys Glu Asn Ala Gly Leu Ser Arg Val Tyr Ser> 530 540 550 560 CAG TGG GCT GGA AAG ACA CAA ATA TTT ATT CCT CTT AAA AAG GAT ATT GTC ACC CGA CCT TTC TGT GTT TAT AAA TAA GGA GAA TTT TTC CTA TAA Gln Trp Ala Gly Lys Thr Gln Ile Phe Ile Pro Leu Lys Lys Asp Ile> 580 590 600 610 TTG TCT GGA AAT ATT GAG TCT GAC ATT GAT ATT GAC AGT TTA GTT ACA AAC AGA CCT TTA TAA CTC AGA CTG TAA CTA TAA CTG TCA AAT CAA TGT Leu Ser Gly Asn Ile Glu Ser Asp Ile Asp Ile Asp Ser Leu Val Thr> 630 640 650 €€0 GAT AAG GTG GTG GCA GCT CTT TTA AGT GAA AAT GAA GCA GGT GTT AAC CTA TTC CAC CAC CGT CGA GAA AAT TCA CTT TTA CTT CGT CCA CAA TTG Asp Lys Val Val Ala Ala Leu Leu Ser Glu Asn Glu Ala Gly Val Asn> 690 700 710 710 680 TTT GCA AGA GAT ATT ACA GAT ATT CAA GGC GAA ACT CAT AAG GCA GAT AAA CGT TCT CTA TAA TGT CTA TAA GTT CCG CTT TGA GTA TTC CGT CTA Phe Ala Arg Asp Ile Thr Asp Ile Gln Gly Glu Thr His Lys Ala Asp> 740 750 760 CAA GAT AAA ATT GAT ATT GAA TTA GAC AAT ATT CAT GAA AGT GAT TCC GTT CTA TTT TAA CTA TAA CTT AAT CTG TTA TAA GTA CTT TCA CTA AGG Gln Asp Lys Ile Asp Ile Glu Leu Asp Asn Ile His Glu Ser Asp Ser> 780 790 AAT ATA ACA GAA ACT ATT GAA AAT TTA AGG GAT CAG CTT GAA AAA GCT TTA TAT TGT CTT TGA TAA CTT TTA AAT TCC CTA GTC GAA CTT TTT CGA Asn Ile Thr Glu Thr Ile Glu Asn Leu Arg Asp Gln Leu Glu Lys Ale>

FIGURE 16 (2 of 5)

820 830 850 860 ACA GAT GAA GAG CAT AAA AAA GAG ATT GAA AGT CAG GTT GAT GCT AAA TGT CTA CTT CTC GTA TTT TTT CTC TAA CTT TCA GTC CAA CTA CGA TTT Thr Asp Glu Glu His Lys Lys Glu Ile Glu Ser Gln Val Asp Ala Lys> 870 880 890 900 AAG AAA CAA AAG GAA GAG CTA GAT AAA AAG GCA ATA AAT CTT GAT AAA TTC TTT GTT TTC CTT CTC GAT CTA TTT TTC CGT TAT TTA GAA CTA TTT Lys Lys Gln Lys Glu Glu Leu Asp Lys Lys Ala Ile Asn Leu Asp Lys> 920 930 940 950 GCT CAG CAA AAA TTA GAT TCT GCT GAA GAT AAT TTA GAT GTT CAA AGA CGA GTC GTT TTT AAT CTA AGA CGA CTT CTA TTA AAT CTA CAA GTT TCT Ala Gln Gln Lys Leu Asp Ser Ala Glu Asp Asn Leu Asp Val Gln Arg> 970 980 990 AAT ACT GTT AGA GAG AAA ATT CAA GAG GAT ATT AAC GAA ATT AAC AAG TTA TGA CAA TCT CTC TTT TAA GTT CTC CTA TAA TTG CTT TAA TTG TTC Asn Thr Val Arg Glu Lys Ile Gln Glu Asp Ile Asn Glu Ile Asn Lys> 1020 1030 1040 1050 GAA AAG AAT TTA CCA AAG CCT GGT GAT GTA AGT TCT CCT AAA GTT GAT CTT TTC TTA AAT GGT TTC GGA CCA CTA CAT TCA AGA GGA TTT CAA CTA Glu Lys Asn Leu Pro Lys Pro Gly Asp Val Ser Ser Pro Lys Val Asp> 1070 1080 1090 1100 AAG CAA CTA CAA ATA AAA GAG AGC CTG GAA GAT TTG CAG GAG CAG CTT TTC GTT GAT GTT TAT TTT CTC TCG GAC CTT CTA AAC GTC CTC GTC GAA Lys Gln Leu Gln Ile Lys Glu Ser Leu Glu Asp Leu Gln Glu Gln Leu> 1110 1130 1140 AAA GAA ACT GGT GAT GAA AAT CAG AAA AGA GAA ATT GAA AAG CAA ATT TTT CTT TGA CCA CTA CTT TTA GTC TTT TCT CTT TAA CTT TTC GTT TAA Lys Glu Thr Gly Asp Glu Asn Gln Lys Arg Glu Ile Glu Lys Gln Ile> 1160 1170 1180 1190 GAA ATC AAA AAA AGT GAT GAA AAG CTT TTA AAA AGT AAA GAT GAT AAA CTT TAG TIT TTT TCA CTA CTT TTC GAA AAT TTT TCA TTT CTA CTA TTT Glu Ile Lys Lys Ser Asp Glu Lys Leu Leu Lys Ser Lys Asp Asp Lys> 1220 1230 GCA AGT AAA GAT GGT AAA GCC TTG GAT CTT GAT CGA GAA TTA AAT TCT CGT TCA TTT CTA CCA TTT CGG AAC CTA GAA CTA GCT CTT AAT TTA AGA Ala Ser Lys Asp Gly Lys Ala Leu Asp Leu Asp Arg Glu Leu Asn Ser>

FIGURE 16 (3 of 5)

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1280 1260 1270 1250 AAA GCT TCT AGC AAA GAA AAA AGT AAA GCC AAG GAA GAA ATA ACC TTT CGA AGA TCG TTT CTT TTT TCA TTT CGG TTC CTT CTT TAT TGG Lys Ala Ser Ser Lys Glu Lys Ser Lys Ala Lys Glu Glu Glu Ile Thr> 1330 1320 1310 AAG GGT AAG TCA CAG AAA AGC TTA GGC GAT TTG AAT AAT GAT GAA AAT TTC CCA TTC AGT GTC TTT TCG AAT CCG CTA AAC TTA TTA CTA CTT TTA Lys Gly Lys Ser Gln Lys Ser Leu Gly Asp Leu Asn Asn Asp Glu Asn> 1370 - ---1380 1360 1350 CTT ATG ATG CCA GAA GAT CAA AAA TTA CCT GAG GTT AAA AAA TTA GAT GAA TAC TAC GGT CTT CTA GTT TTT AAT GGA CTC CAA TTT TTT AAT CTA Leu Met Met Pro Glu Asp Gln Lys Leu Pro Glu Val Lys Lys Leu Asp> 1430 1420 1410 1400 AGC AAA AAA GAA TTT AAA CCT GTT TCT GAG GTT GAG AAA TTA GAT AAG TCG TTT TTT CTT AAA TTT GGA CAA AGA CTC CAA CTC TTT AAT CTA TTC Ser Lys Lys Glu Phe Lys Pro Val Ser Glu Val Glu Lys Leu Asp Lys> 1470 1460 1450 ATT TTC AAG TCT AAT AAC AAT GTT GGA GAA TTA TCA CCG TTA GAT AAA TAA AAG TTC AGA TTA TTG TTA CAA CCT CTT AAT AGT GGC AAT CTA TTT Ile Phe Lys Ser Asn Asn Asn Val Gly Glu Leu Ser Pro Leu Asp Lys> 1520 1510 1500 1490 TCT TCT TAT AAA GAC ATT GAT TCA AAA GAG GAG ACA GTT AAT AAA GAT AGA AGA ATA TTT CTG TAA CTA AGT TTT CTC CTC TGT CAA TTA TTT CTA Ser Ser Tyr Lys Asp Ile Asp Ser Lys Glu Glu Thr Val Asn Lys Asp> 1570 · 1560 1550 GTT AAT TTG CAA AAG ACT AAG CCT CAG GTT AAA GAC CAA GTT ACT TCT CAA TTA AAC GTT TTC TGA TTC GGA GTC CAA TTT CTG GTT CAA TGA AGA Val Asn Leu Gln Lys Thr Lys Pro Gln Val Lys Asp Gln Val Thr Ser> 1620 1600 1610 1590 TTG AAT GAA GAT TTG ACT ACT ATG TCT ATA GAT TCC AGT AGT CCT GTA AAC TTA CTT CTA AAC TGA TGA TAC AGA TAT CTA AGG TCA TCA GGA CAT Leu Asn Glu Asp Leu Thr Thr Met Ser Ile Asp Ser Ser Ser Pro Val> 1670 1660 1650 1640 TTT TTA GAG GTT ATT GAT CCA ATT ACA AAT TTA GGA ACT CTT CAA CTT AAA AAT CTC CAA TAA CTA GGT TAA TGT TTA AAT CCT TGA GAA GTT GAA Phe Leu Glu Val Ile Asp Pro Ile Thr Asn Leu Gly Thr Leu Gln Leu>

FIGURE 16 (4 of 5)

1720 1690 1700 ATT GAT TTA AAT ACT GGT GTT AGG CTT AAA GAA AGC ACT CAG CAA GGC TAA CTA AAT TTA TGA CCA CAA TCC GAA TTT CTT TCG TGA GTC GTT CCG Ile Asp Leu Asn Thr Gly Val Arg Leu Lys Glu Ser Thr Gln Gln Gly> 1770 1750 1760 1740 1730 ATT CAG CGG TAT GGA ATT TAT GAA CGT GAA AAA GAT TTG GTT GTT ATT TAA GTC GCC ATA CCT TAA ATA CTT GCA CTT TTT CTA AAC CAA CAA TAA Ile Glm Arg Tyr Gly Ile Tyr Glu Arg Glu Lys Asp Leu Val Val Ile> 1800 1780 AAA ATG GAT TCA GGA AAA GCT AAG CTT CAG ATA CTT GAT AAA CTT GAA TTT TAC CTA AGT CCT TTT CGA TTC GAA GTC TAT GAA CTA TTT GAA CTT Lys Met Asp Ser Gly Lys Ala Lys Leu Gln Ile Leu Asp Lys Leu Glu> 1850 1860 1840 1870 1830 AAT TTA AAA GTG GTA TCA GAG TCT AAT TTT GAG ATT AAT AAA AAT TCA TTA AAT TTT CAC CAT AGT CTC AGA TTA AAA CTC TAA TTA TTT TTA AGT Asn Leu Lys Val Val Ser Glu Ser Asn Phe Glu Ile Asn Lys Asn Ser> 1890 1900 1910 1920 1880 TCT CTT TAT GTT GAT TCT AAA ATG ATT TTA GTA GCT GTT AGG GAT AAA AGA GAA ATA CAA CTA AGA TTT TAC TAA AAT CAT CGA CAA TCC CTA TTT Ser Leu Tyr Val Asp Ser Lys Met Ile Leu Val Ala Val Arg Asp Lys> 1940 1950 1960 1930 GAT AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA CTA TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT Asp Ser Ser Asn Asp Trp Arg Leu Ala Lys Phe Ser Pro Lys Asn Leu> 1990 2000 1980 • • GAT GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT CTA CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA Asp Glu Phe Ile Leu Ser Glu Asn Lys Ile Met Pro Phe Thr Ser Phe> 2060 2030 2040 2050 2020 TCT GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA AGA CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT Ser Val Arg Lys Asn Phe Ile Tyr Leu Gln Asp Glu Phe Lys Ser Leu> 2080 2090 2100 2070 GTT ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG TA CAA TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC AT

FIGURE 16 (5 of 5)

Val Ile Leu Asp Val Asn Thr Leu Lys Lys Val Lys Xxx>

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1	ATGAAAAAAT	TGTTACTAAT	CITTAGITTI	TITCITATIT	CITIONATOO	WILLCCICII
61	AATTCAAGGG	AAGTTGATAA	GGAAAAATTA	AAGGATTTTG	TTAATATGGA	TCTTGAGTTT
121	GTAAACTATA	AAGGTCCTTA	TGATTCTACA	AATACATATG	AACAAATAGT	AGSTATIGGT
. 181	GAGTTTTTAG	CAAGACCATT	GATTAATTCC	AATAGCAACT	CAATITATTA	TGGTAAATAT
241	ATAATTAATT	GATTTATTGA	TGATCAAGAT	AAAAAAGCAA	GCGTTGATGT	TTTTTCTATT
301	GGTAGTAGGT	CACAGCTTGA	CAGTATATTG	AATCTAAGAA	GAATTCTTAC	AGGGTATTIG
361	ATAAAGTCTT	TTGATTATGA	AAGATCTAGT	GCTGAATTAA	TTGCTAAGGT	TATTACAATA
421	CATAATGCTG	TTTATAGAGG	GGATTTAAAT	TATTATAAAG	AGGTTTATAT	TGAGGCTGCT
481	TTAAAGTCTT	TAACTAAAGA	AAATGCAGGT	CTTTCTAGAG	TGTACAGTCA	ATGGGCTGGA
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	TATTTTTAT	CTGGAAAAGT	TGAGTCTGAC
601	ATTGATATTG	ACAGITIGGI	TACAGATAAG	GTTGTGGCAG	-CICITITAAG	CGAGAATGAA
661	GCAGGTGTTA	ACTITGCAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAAGCAGAT
721	CAAGATAAAA	TIGATATIGA	ATTAGATAAT	GTTCATAAAA	GTGATTCCAA	TATAACAGAG
781	ACTATTGAGA	ATTTAAGAGA	TCAGCTTGAA	AAGGCTACAG	ATGAAGAGCA	TAGAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAAGAAG	AACTAGATAA	AAAGGCAATC
901	GATCTTGATA	AAGCCCAACA	AAAATTAGAT	TCTTCTGAAG	ATAATTTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGAT	TCAAGAGGAT	ATTGACGAGA	TTAATAAAGA	AAAGAATTTG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AGCTACAAAT	AAAAGAGAGT
1081	CTAGAAGACT	TGCAGGAACA	GCTTAAAGAA	ACTAGCGATG	AAAATCAAAA	AAGAGAAATT
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAGTGAT	GAAGAACTTT	TAAAAAGTAA	AGATCCTAAA
1201	GCATTAGATC	TTAATGGAGA	TTTAAATTCT	AAAGTTTCTA	GTAAAGAAAA	AATTAAAGGC
	AAAGAAGGAG					
1321	GAAAATCTTA	TGAGGCCGGA	AGATCAAAAA	TTATCTGAGG	TTAAAAATT	AGATAGTAAA
	AATTTAA					
1441	AATGAGATTA					
1501		ATAATAAAGA				
1561		TAAATCAAGA				
1621		TIGATCCTAT				
	GGTGTTAGAC					
	GAAAAAGATT					
	AAACTTGAGA					
1861	CTTTATGTTG					
1921		TTTCTCCTAA				
	CCTTTTACTA					GTTTAAAAGT
2041	CTTATTACTT	TAGATGTAAA	TACTTTAAAA	AAAGTTAAGT	A	

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1141	GWWWWGCWWW	TIGAAAICAA	AAAAAATTTAT	ململمك لا لا تا الا	TYPE A A A A A MARK	
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1	ATGAAAAAAA	TGTTACTAAT	CTTTAGTTTT	TITCITGITT	TTTTAAATGG	ATTTCCTCTT
61	AATGCAAGGG	AAGTTGATAA	GGAAAAATTA	AAGGACTTTG	TTAATATGGA	TCTTGAATTT
121	GTTAATTACA	AGGGTCCTTA	TGATTCTACA	AATACATATG	AACAAATAGT	AGGTATTGGG
181	GAGTTTTTAG	CAAGGCCGTT	GATCAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
241	TTTGTTAATA	GATTTATTGA	CGATCAAGAT	AAAAAAGCAA	GTGTTGATAT	TTTTTCTATT
301	GGTAGTAAGT	CAGAGCTTGA	TAGTATATTA	AATCTAAGAA	GAATTCTTAC	AGGGTATTTA
361				GCGGAATTAA		
421				TATTACAAAG		
481				CTTTCTAGGG		
541	AAGACACAAA	TATTTATTCC	TCTTAAAAAG	<b>TATTTTTAT</b>	CIGGAAATGI	TGAGTCTGAC
601	ATTGATATTG					
661				GACATTCAAG		
	CAAGATAAAA					
781	ACTATTGAGA					
841	ATTGAAAGTC	AGGITGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901						
961				ATTAACGAGA		
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTACAAAT	AAAAGAGAGC
1081				ACTGGTGATG		
1141				GAAAAGCTTT		
1201				GATCGAGAAT		
1261				ATAACCAAGG		
1321				ATGCCAGAAG		
1381				CCTGTTTCTG		
1441				TTATCACCGT		
1501	GACATTGATT	CAAAAGAGGA	GACAGTTAAT	AAAGATGTTA	ATTTGCAAAA	GACTAAGCCT
1561	CAGGTTAAAG	ACCAAGTTAC	TTCTTTGAAT	GAAGATTTGA	CTACTATGTC	TATAGATTCC
1621	AGTAGTCCTG	TATTTTTAGA	GGTTATTGAT	CCAATTACAA	ATTTAGGAAC	TCTTCAACTT
1681				GAAAGCACTC		
1741	GGAATTTATG	AACGTGAAAA	AGATTTGGTT	GTTATTAAAA	TGGATTCAGG	AAAAGCTAAG
1801				AAAGTGGTAT		
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	GATAGTAGTA					
1981				AGCTTTTCTG		
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2101	TAAAGCC					

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	ATGAAAAAA					
	AATGCAAGGG					
	GTTAATTACA					
181	GAGTTTTTAG	CAAGGCCGTT	GATCAATTCC	AATAGTAATT	CAAGTTATTA	TGGTAAATAT
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	GGTAGTAAGT					
361	ATGAAGTCTT					
421	TATAATGCTG	TTTATAGAGG	AGATTTAGAT	TATTACAAAG	AGTTTTATAT	TGAGGCTTCT
481	TTGAAGTCTT	TGACTAAAGA	AAATGCAGGT	CTTTCTAGGG	TGTACAGTCA	ATGGGCTGGG
	<b>AAGACACAAA</b>					
601	ATTGATATTG	ATAGTTTGGT	TACAGATAAG	GTGGTGGCAG	CTCTTTTAAG	TGAGAATGAA
						TAAAGCAGAT .
	CAAGATAAAA					
781	ACTATTGAGA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	TAAAAAAGAG
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	CAAAAGGAAG	AATTAGATAA	AAAGGCAATT
901	GATCTTGATA	AAGCTCAACA	AAAATTAGAT	TTTGCTGAAG	ATAATCTAGA	TATTCAAAGG
961	GATACTGTTA	GAGAGAAGCT	TCAAGAAAAT	ATTAACGAGA:	CTAATAAGGA	AAAGAATTTA
1021	CCAAAGCCTG	GTGATGTAAG	TTCTCCTAAG	GTTGATAAGC	AGTTGCAGAT	AAAAGAGAGT
1081	CTAGAAGATT	TGCAAGAGCA	GCTTAAAGAA	GCTAGTGATG	AAAATCAAAA	AAGAGAAATA
1141	GAAAAGCAAA	TTGAAATCAA	AAAAAATGAT	GAAGAACTTT	AATAAAATT	AGATCATAAA
1201	GCATTAGATC	TTAAGCAAGA	ATTAAATTCT	AAAGCTTCTA	GTAAAGAAAA	AATTGAAGGC
1261	GAAGAAGAGG	ATAAAGAATT	AGATAGTAAA	AAAAATTTAG	AGCCTGTTTC	TGAGGCTGAT
1321	AAAGTAGATA	AAATTTCCAA	GTCTAACAAC	AATGAGGTTA	GTAAATTATC	CCCGTTAGAT
1381	GAGCCTTCTT	ATAGCGACAT	TGATTCGAAA	GAGGGTGTAG	ATAACAAAGA	TGTTGATTTG
1441	CAAAAAACTA	AACCCCAAGT	TGAAAGTCAA	CCTACTTCGT	TAAATGAAGA	CTTGATTGAT
1501	GTGTCTATAG	ATTCCAGTAA	TCCTGTCTTT	TTAGAGGTTA	TCGATCCGAT	TACAAATTTA
1561	GGAACGCTTC	AACTTATTGA	TTTGAATACC	GGTGTTAGAC	TTAAAGAAAG	TGCTCAACAA
1621.	GGTATTCAGC	GATATGGAAT	TTATGAACGT	GAAAAAGATT	TGGTTGTTAT	TAAAATAGAT
1681	TCAGGAAAAG	CTAAGCTTCA	GATACTTGAT	AAACTCGAGA	ATTTAAAAGT	GATATCAGAG
1741	TCTAATTTTG	AGATTAATAA	AAATTCATCT	CTTTATGTTG	ACTOTAGAAT	GATTITAGTA
1801	GTTGTTAAGG	ACGATAGTAA	TGCTTGGAGA	TTGGCTAAAT	TITCTCCTAA	AAATTTAGAT
1861	GAATTTATTC	TGTCAGAAAA	TAAAATTTTG	CCTTTTACTA	GCTTTGCTGT	GAGAAAGAAT
1921	TTTATTTATT	TGCAAGATGA	ACTTAAAAGC	TTAGTTACTT	TAGATGTAAA	TACTTTAAAA
1981	AAAGTTAAGT	A		-		

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1	ATGAAAAAA	TGTTACTAAT	CTTTAGTTTT	TTTCTTATTT	TTTTGAATGG	ATTICCICIT
61	ADDRACCA	AAGTTGATAA	GGAAAAATTA	AAGGATTTIG	TTAATATGGA	TCTTGAGTTT
121	GTAAATTATA	AAGGTCCTTA	TGATTCTACA	AATACGTATG	AACAAATAGT	GGGTATTGGG
		CAAGACCGCT		AATAGCAACT	CAAGTTATTA	TGGCAAATAT
241	TTTATTAATA	GATTTATTGA	TGATCAAGAT		GTGTTGATGT	
301	AGCAGCAAAT	CAGAGCTTGA	CAGTATATTG	AATTTAAGAA	GAATTCTTAC	AGGGTATATA
		TCGATTATGA		GCAGAATTAA	TIGCTAAGGT	TATTACAATA
421	TATAATGCTG	TTTATAGAGG	AGATTTGGAT		GGTTTTATAT	
481	TTGAAGTCTT	TAACTAAAGA	AAACGCAGGT			GTGGGCTGGA
541	AAGACTCAAA	TATTTATTCC	TCTTAAAAAG	GATATTTTGT	CTGGAAATAT	TGAATCTGAC
601	ATTGATATTG	ACAGTTTGGT	TACAGATAAG	GTGATAGCAG	CTCTTTTAAG	CGAAAATGAA
661	GCAGGCGTTA	ACTITGCAAG	AGATATTACA	GATATTCAAG	GCGAAACTCA	TAAGGCAGAT
721	CAAGATAAGA	TTGATACTGA	ATTAGACAAT	ATCCATGAAA	GCGATTCTAA	TATAACAGAA
781	ACTATTGAAA	ATTTAAGGGA	TCAGCTTGAA	AAAGCTACAG	ATGAAGAGCA	Taaaaaagag
841	ATTGAAAGTC	AGGTTGATGC	TAAAAAGAAA	.GAAAAGGAAG	AGCTAGATAA	AAAGGCAATC
901	AATCTTGATA	AAGCTCAGCA	AAAATTAGAC	TCTGCTGAAG	ATAATTTAGA	TGTTCAAAGA
961	GATACTGTTA	GAGAGAAAAT	TCAAGAGGAT	ATTAATGAGA	TTAATAAGGA	AAAGAATITG
1021	CCAAAACCTG	GTGATGTAAG	TTCTCCTAAA	GTTGATAAGC	AACTGCAAAT	AAAAGAGAGT
1081	CTAGAAGATT	TGCAGGAGCA	GCTTAAAGAA	GCTGGTGATG	AAAATCAGAA	AAGAGAAATT
1141	GAGAAGCAAA	TTGAAATCAA	AAAAAGGGAC	GAAGAACTTT	TAAAAAGTAA	AGATGGCAAA
1201	GTAAGTAAAG	ATTATGAAGC	ATTAGATCTT	GATCGAGAAT	TATCCAAAGC	TTCTAGTAAA
1261	GAAAAAAGTA	AGGTCAAGGA	AGAAGAAATA	ACTAAAGGTA	AATCACGGGC	AAGCTTAGGC
1321	GATTTGAATA	ATGATAAAAA	CCTTATGTTG	CCAGAAGATC	AAAAATTACC	TGAAGATAAA
1381	AAATTGGATA	GTAAATTAGA	TGGTAAAAA	GAATTTAAAC	CAGTITCTGA	GGTTGAAAAA
		TTTCCAAGTC				
		ATGATATTGA				
1561		CTAAAGTTAA				
1621		TGTCTATAGA				
		GAACCCTGCA				
		GCATTCAGCG				
		CAGGAAAGGC				
1861		CTAATTITGA				
1921		CTGTTAGAGA				
1981		TGGATGAGTT				
2041		TATTTTAAAA`.		GATGAGCTTA	AAAATCTAGT	TATTTTAGAT
2101	GTAAATACTT	TAAAAAAAGT	TAAGTA			

### K48 OSP A/PGAU OSP A FUSION

39/133

20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TTT TTT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 60 70 90 TGT AAG CAA AAT GTT AGC AGC CTT GAT GAA AAA-AAT AGC GTT TCA GTA... ACA TTC GTT TTA CAA TCG TCG GAA CTA CTT TTT TTA TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 110 120 130 GAT TTA CCT GGT GGA ATG ACA GTT CTT GTA AGT AAA GAA AAA GAC AAA CTA AAT GGA CCA CCT TAC TGT CAA GAA CAT TCA TTT CTT TTT CTG TTT Asp Leu Pro Gly Gly Met Thr Val Leu Val Ser Lys Glu Lys Asp Lys> 160 170 180 GAC GGT AAA TAC AGT CTA GAG GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCA TTT ATG TCA GAT CTC CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Ser Leu Glu Ala Thr Val Asp Lys Leu Glu Leu Lys> 210 220 230 GGA ACT TCT GAT AAA AAC AAC GGT TCT GGA ACA CTT GAA GGT GAA ALA CCT TGA AGA CTA TTT TTG TTG CCA AGA CCT TGT GAA CTT CCA CTT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Thr Leu Glu Gly Glu Lys> 260 270 ACT GAC AAA AGT AAA GTA AAA TTA ACA ATT GCT GAT GAC CTA AGT CAA TGA CTG TTT TCA TTT CAT TTT AAT TGT TAA CGA CTA CTG GAT TCA GTT Thr Asp Lys Ser Lys Val Lys Leu Thr Ile Ala Asp Asp Leu Ser Glm> 300 310 320 ACT AAA TTT GAA ATT TTC AAA GAA GAT GCC AAA ACA TTA GTA TCA AAA TGA TTT AAA CTT TAA AAG TTT CTT CTA CGG TTT TGT AAT CAT AGT TTT Thr Lys Phe Glu Ile Phe Lys Glu Asp Ala Lys Thr Leu Val Ser Lys> .340 350 360 370 AAA GTA ACC CTT AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAC GAA TTT CAT TGG GAA TIT CTG TTC AGT AGT TGT CTT TTT AAG TTG CTT Lys Val Thr Leu Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu>

FIGURE 23 (1 of 3)

### K48 OSP A/ PGAU OSPA FUSION

	390		_	40	0	•	4	10			420	•	•	43	0
* AG	* TDD	CAA	ACA.	TCT	GAA"	- AAA	ACA	ATA	GTA	AGA	GCA	AAT	GGA	ACC	AGA
														TGG	
Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
	4	40			450		•	46	0		. 4	70			480
•	•	•		•	*		•		•	•		•		•	•
·CTT															
															CTT
Leu	Glu	Tyr	Thr	Asp	Ile	Lys	Ser	Asp	GIĀ	Ser	Gly	Lys	Ala	Lys	Glu>
		49	0		5	00			510			52	20	•	
	•		• .	•		•		•	•		•		•	•	
														GGC	
															TIT
Val	Leu	Lys	Asp	Phe	Thr	Leu	GIU	GIĀ	Inr	ren	AIS	YIS	Asp	GIÅ	Lys>
530			540			55	50		9	60			570		
•		•	•		•		•	•		•		•	•		•
														AAC	
														TTG	TAA Ile>
Thr	Inr	ren	Lys	val	inr	GIU	GIY	1111	vaı	AGI	reu	Ser	Lys	ASI	:16>
- 51	BO			590			600		_	61	10	_	6	520	•
	•	<b>.</b>		•	8 T	*	•	CCA	*		•	* ~~~		•	».
TTA	AAA		GGA	GAA			GTT			GAT	GAC		GAC	ACT	
ATT TAA	AAA TTT	AGG	GGA CCT	GAA CTT	TAT	TGT	GTT CAA	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	TGA
ATT TAA	AAA TTT Lys	AGG	GGA CCT	GAA CTT Glu	TAT Ile	TGT	GTT CAA Val	CGT Ala	GAA	GAT CTA	GAC CTG Asp	AGA	GAC CTG	ACT TGA Thr	TGA Thr>
ATT TAA	AAA TTT	AGG	GGA CCT	GAA CTT Glu	TAT	TGT	GTT CAA Val	CGT	GAA	GAT CTA	GAC CTG	AGA	GAC CTG	ACT TGA	TGA Thr>
TTA AAT Leu	AAA TTT Lys	AGG Ser	GGA CCT Gly	GAA CTT Glu	TAT Ile 40	TGT Thr	GTT CAA Val	CGT Ala 650	GAA Leu	GAT CTA Asp	GAC CTG Asp	AGA Ser	GAC CTG Asp	ACT TGA Thr	TGA Thr>
TTA AAT Leu  * CAG	AAA TTT Lys 630 GCT	AGG Ser ACT	GGA CCT Gly	GAA CTT Glu 64	TAT Ile 40 * ACT	TGT Thr GGA	GTT CAA Val	CGT Ala 650 TGG	GAA Leu GAT	GAT CTA Asp	GAC CTG Asp 660	AGA Ser ACT	GAC CTG Asp	ACT TGA Thr	TGA Thr> 70 TTA
TTA AAT Leu CAG GTC	AAA TTT Lys 630 GCT CGA	AGG Ser ACT TGA	GGA CCT Gly	GAA CTT Glu 64	TAT Ile 40 * ACT TGA	TGT Thr • GGA CCT	GTT CAA Val AAA TTT	CGT Ala 650 TGG ACC	GAA Leu GAT CTA	GAT CTA Asp TCA AGT	GAC CTG Asp 660 AAA TTT	AGA Ser ACT TGA	GAC CTG Asp * TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA
TTA AAT Leu CAG GTC	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA	GGA CCT Gly	GAA CTT Glu 64	TAT Ile 40 * ACT TGA	TGT Thr • GGA CCT	GTT CAA Val AAA TTT	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA	GAT CTA Asp TCA AGT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA	GAC CTG Asp * TCT AGA	ACT TGA Thr 67 ACT TGA	TGA Thr> 70 TTA AAT
TTA AAT Leu CAG GTC GIn	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys	TAT Ile  40 ACT TGA Thr  690	TGT Thr • GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp	GAA Leu GAT CTA Asp	GAT CTA Asp TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720
TTA AAT Leu CAG GTC GIn	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys	TAT Ile 40 * ACT TGA Thr 690 *	TGT Thr GGA CCT Gly	GTT CAA Val AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7	GAA Leu GAT CTA Asp	GAT CTA ASP TCA AGT Ser	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710	GAC CTG Asp TCT AGA Ser	ACT TGA Thr 67 ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA
TTA AAT Leu CAG GTC GIn ACA TGT	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680 AGT TCA	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG	TGT Thr GGA CCT Gly AAA TTT	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 • ACA	GAT CTA ASP TCA AGT Ser CAA GTT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC	GAC CTG Asp TCT AGA Ser TTT	ACT TGA Thr TGA Thr ACT TGA TGA	TGA Thr>  O TTA AAT Leu>  720 AAA TTT
TTA AAT Leu CAG GTC GIn ACA TGT	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680 AGT TCA	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG	TGT Thr GGA CCT Gly AAA TTT	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 • ACA	GAT CTA ASP TCA AGT Ser CAA GTT	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC	GAC CTG Asp TCT AGA Ser TTT	ACT TGA Thr TGA Thr ACT TGA TGA	TGA Thr> 70 TTA AAT Leu> 720 AAA
TTA AAT Leu CAG GTC GIn ACA TGT	AAA TTT Lys 630 GCT CGA Ala	AGG Ser ACT TGA Thr 680 AGT TCA Ser	GGA CCT Gly AAA TTT Lys	GAA CTT Glu 6. AAA TTT Lys	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT	GTT CAA Val AAA TTT Lys AAA TTT	CGT Ala 650 TGG ACC Trp 7 ACT TGA	GAA Leu GAT CTA Asp 00 • ACA	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys	AGA Ser ACT TGA Thr 710 GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT	ACT TGA Thr TGA Thr ACT TGA TGA	TGA Thr>  O TTA AAT Leu>  720 AAA TTT
TTA AAT Leu CAG GTC Gln ACA TGT Thr	AAA TTT Lys 630 GCT CGA Ala ATT TAA Ile	AGG Ser ACT TGA Thr 680 AGT TCA Ser	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG ASD	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys	GTT CAA Val AAA TTT Lys AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA ASP 00 ACA TGT Thr	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA Thr	TGA Thr>  TTA AAT Leu>  720 AAA TTT Lys>
TTA AAT Leu  CAG GTC Gln ACA TGT Thr	AAA TTT Lys 630 GCT CGA Ala ATT TAA Ile	AGG Ser ACT TGA Thr 680 AGT TCA Ser 7	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG ASD	TAT Ile 40 *ACT TGA Thr 690 *AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys 740	GTT CAA Val AAA TTT Lys AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA ASP 00 ACA TGT Thr 750	GAT CTA ASP TCA AGT Ser CAA GTT Gln	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val 7	GAC CTG Asp TCT AGA Ser TTT AAA Phe	ACT TGA Thr 67 ACT TGA Thr ACT TGA Thr	TGA Thr> 70 TTA AAT Leu> 720 AAA TTT Lys>
TTA AAT Leu  CAG GTC GIn  ACA TGT Thr	AAA TTT Lys 630 GCT CGA Ala ATT TAA Ile	AGG Ser ACT TGA Thr 680 AGT TCA Ser 7	GGA CCT Gly AAA TTT Lys GTT CAA Val	GAA CTT Glu 6 AAA TTT Lys AAC TTG ASD	TAT Ile 40 * ACT TGA Thr 690 * AGC TCG Ser	TGT Thr GGA CCT Gly AAA TTT Lys 740	GTT CAA Val AAA TTT Lys AAA TTT Lys	CGT Ala 650 TGG ACC Trp 7 ACT TGA Thr	GAA Leu GAT CTA Asp 00 ACA TGT Thr 750 GAC	GAT CTA ASP TCA AGT Ser CAA GTT Gln TCC AGG	GAC CTG Asp 660 AAA TTT Lys CTT GAA Leu	AGA Ser ACT TGA Thr 710 GTG CAC Val 7	GAC CTG ASP TCT AGA Ser TTT AAA Phe 60 ACC TGG	ACT TGA Thr 67 ACT TGA Thr TGA Thr	TGA Thr>  TTA AAT Leu>  720 AAA TTT Lys>

FIGURE 23 (2 of 3)

K48 OSPA / PGAU OSP A FUSION

770 780 790 800 810

GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT
CTT CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA
Glu Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala>

820 TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 23 (3 of 3)

## B-31 OSP A /PGAU OSP A FUSION

			•			20			30			4	0		
	•		.0	•		•		•	•		•		•	•	•
ATG	AAA	AAA	TAT	TTA	TTG	GGA	AŢA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
mac.	THY.	للملحك	ልጥል	TAA	AAC	CCT	TAT	CCA	GAT	TAT	AAT	CGG	AAT	TAT	CGT
Met	Lys	Lys	Tyr	Leu'	Leu	Gly	Ile	Gly	Leu	11e	Leu	ATS	Leu	TTG	Ala>
			<b>C</b> 0			7	0			80	•		90		
50		•	60 •		•		*	*		•		•	. •		• ,
TGC	DAA	CAA	AAT	GTT	AGC	AGC	CTT	GAT	GAA	AAA	ĄAC	AGC	GCT	TCA	GTA
3.00		CTT	TTA	CAA	TCG	TCG	GAA	CTA	CTT	TTT	TIG	TCG	CGA	AGT	CAT
Cys	Lys	Gln	Asn	Val	Ser	Ser.	Leu	Asp	Glu	Lys	Asn	Ser	Ala	Ser	Val>
					•		120	-	•	1.	30			140	
1	00			110		•	120		•		*	•		*	
CAT	TTC	CCT	GGT	GAG	ATG	AAA	GTT	CTT	GTA	AGT	AAA	GAA	AAA	GAC	AAA
<b>ር</b> ሞእ	AAC	CCA	CCA	CTC	TAC	TTT	CAA	GAA	CAT	TCA	TTT	CTT	TTT	CTG	TTT
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Lys	Glu	Lys	Asp	Lys>
					- 0			170			180			3	90
_	150			1.	60	*	•	+		•	*		•	_	•
CNC	- CC1	, אאני	". ግልጥ::	AGT	СТА	AAG	GCA	ACA	GTA	GAC	AAG	ATT	GAG	CTA	AAA
CTC	CCA	الند	ATG	TCA	GAT	TTC	CGT	TGT	CAT	CTG	TTC	TAA	CIC	GAT	TTT
Asp	Gly	Lys	Tyr	Ser	Leu	Lys	Ala	Thr	Val	Asp	Lys	Ile	Glu	Leu	Lys>
								ว	20			230			240
		200	,	•	210		•	. 2	*	•		*		•	
CCI	אריז	ר הרת ה	רבם י	AAA	GAC	AAT	GGT	TCT	GGA	GTG	CTT	GAA	GGT	ACA	AAA
~~	TC	ACI	CTA	TTT	CTG	TTA	CCA	AGA	CCI	, CYC	GAA	CII	CCA	TGT	T-I-I
Gly	Th	. Sei	Asp	Lys	Asp	Asn	Gly	Ser	Gly	Val	Leu	Glu	Gly	Thr	Lys>
						260			270	1		2	во		
			250	•		260		•	270	,	•	2	*	•	
Gh'	ים ומסיד	~ AA	A AGT	ኋልል ገ	. GCA	AAA	TTA	AC	AT?	r GCI	GAC	GAT	CTA	AGT	AAA '
C41	A CTY	ملىك ت	r TC	TTT	CGI	TTI	'AAI	TG	LAT 7	A CGA	CIC	CTA	GAT	, LC	LIL
As	As	p Ly:	s Sex	Lys	a Ala	Lys	Lev	Thi	c Ile	e Ala	Asp	) Asp	Lev	Ser	: Lys>
			201			-	10			320			330	) _	
290		₩.	309	•	•	-	*		•	*		•	•	•	•
àС	C AC	7 TT	C GA	A CT	r TT	AA A	A GAZ	A GA	r GG	CAA	A AC	A TTA	GTC	TC	A AGA
TC:	C TC	aa m	C CT	T GA	A AA	L LL	r cr	r ct.	A CC	G TT	r TG	r aa:	CAU	, AG	LICI
Th	r Th	r Ph	e Gl	u Lei	u Lei	Ly:	s Gl	ı As	p Gl	y Ly:	s Th	r Lei	ı Val	l Se:	r AIG>
				350			36	n			370	٠		380	
	340			350		•	30	•	•		•		•	•	
12.21	LA GT	A AC	T TC	T AG	A GA	C AA	A AC	A TC	A AC	A GA	T GA	TA A	G TT	C AA	T GAA
ጥባ	ידי כז	ነጥ ጥር	'A AG	A TC	T CT	G TT	T TG	T AG	TTG	T CT	A CT	T TA	CAA	G TT	A CII
L	s Va	al Se	er Se	r Ar	g As	p Ly	s Th	r Se	r Th	r As	p Gl	и ∙Ме	t Ph	e As	n Glux

FIGURE 24 (1 of 3)

### B-31 OSP A/ PGAU OSP A FUSION

		390		•	4	00		•	410		•	420			4	30
	AAA	GGT	GAA	TTG	TCT	GCA	AAA	ACC	ATG	ACA	AGA	GAA	AAT	GGA	ACC	AAA
	TTT	CCA	CTT	AAC	AGA	CGT	TTT	TGG	TAC	TGT	TCT	CTT	TTA	CCT	TGG	TTT
	Lys	Gly	Glu	Leu	Ser	Ala	Lys	Thr	Met	Thr	Arg	Glu	Asn	Gly	Thr	Lys>
. •			440			450			41	50		4	470			460
	•				•	•		•		•	•		•		•	•
															AAA	
															TTT	CTT Glu>
	Den	Gru	ıyı	1111	GIU	Mec	Lys	361	rsp	GIY	1111	GIY	Lys	WIS	∴ys	G±u>
			4	90			500			510			52	20		
		•		•			•		•	•		•		•	•	
	GTT	TTA	AAA	AAG	TTT	ACT	CTT	GAA	GGA	AAA	GTA	GCT	AAT	GAT	AAA	GTA
	UAA Ual	AAT	TIT	Tyc	AAA	TOA	LAN	Cli	CLT	Tir	CAT	CGA	TTA	CTA	TTT	CAT Val>
	V = 1	Dea	Lys		FILE	1111	Deu	<b>G1</b> 0	Gly	Lys	AGT.	VIG	ASI	ASP	_ys	AST>
!	530			540			55	50		5	560			570		
	•		•	•		•		•	•		•		•	•		•
	ACA	TTG	CTT	Car	AAA	CTT	GGA	ACC	CAA	ACT	TTA	AGT	AAG	GAA	ATT TAA	GCA
	Thr	Leu	Glu	Val	LVS	Glu	Glv	Thr	Val	Thr	Len	Ser	TAC	CIT	TAA	Ala>
													د ړه	914	=	VIC>
		_		_												
	- 58	30		5	90			600		_	. 61	0		6	520	
		•	. • • •		•	<b>2</b> C2	* .	•	· Стт	• 117		•	*		•	
	AAA	• TCT	GGA CCT	GAA	GTA	ACA TGT	GTT	GCT	CTT	• AAT TTA	GAC	ACT	AAC TTG	ACT	ACT	CAG
٠	AAA TTT	• TCT AGA	CCT	GAA CTT	GTA CAT	TGT	CAA	GCT CGA	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	GTC
	AAA TTT	TCT AGA Ser	CCT	GAA CTT	GTA CAT Val	TGT Thr	CAA	GCT CGA Ala	GAA Leu	TTA	GAC CTG	ACT TGA Thr	TTG	ACT TGA	ACT TGA Thr	GTC Glm>
٠	AAA TTT	• TCT AGA	CCT	GAA CTT	GTA CAT	TGT Thr	CAA	GCT CGA Ala	GAA	TTA	GAC CTG	ACT TGA	TTG	ACT TGA	ACT TGA	GTC Glm>
•	AAA TTT Lys	TCT AGA Ser 630	CCT	GAA CTT Glu	GTA CAT Val	TGT Thr	CAA Val	GCT CGA Ala	GAA Leu 550	TTA Asn	GAC CTG Asp	ACT TGA Thr	TTG Asn	ACT TGA Thr	ACT TGA Thr	GTC Glm>
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630 ACT	CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT	TGT Thr 10 • GGC CCG	CAA Val GCA CGT	GCT CGA Ala TGG	GAA Leu 50 GAT	TTA Asn TCA AGT	GAC CTG Asp + AAA TTT	ACT TGA Thr 660 ACT TGA	TTG ASD TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 67 TTA AAT	GTC Gln> 70 * ACA TGT
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630 ACT	CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT	TGT Thr 10 • GGC CCG	CAA Val GCA CGT	GCT CGA Ala TGG	GAA Leu 50 GAT	TTA Asn TCA AGT	GAC CTG Asp * AAA TTT	ACT TGA Thr 660 ACT TGA	TTG ASD TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 67 TTA AAT	GTC Glm> '0 *
	AAA TTT Lys • GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT	GAA CTT Glu • AAA TTT	GTA CAT Val 64 ACT	TGT Thr 10 • GGC CCG	CAA Val GCA CGT	GCT CGA Ala TGG	GAA Leu 50 GAT	TTA Asn TCA AGT Ser	GAC CTG Asp * AAA TTT	ACT TGA Thr 660 ACT TGA Thr	TTG ASD TCT AGA	ACT TGA Thr ACT TGA	ACT TGA Thr 67 TTA AAT	GTC Gln> 70 * ACA TGT
	AAA TTT Lys • GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys	GAA CTT Glu • AAA TTT Lys	GTA CAT Val 64 ACT TGA Thr	TGT Thr 10 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC TIP	GAA Leu 550 GAT CTA Asp	TTA Asn TCA AGT Ser	GAC CTG Asp * AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TTG Asn TCT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 67 TTA AAT Leu	GTC Glm> 70 ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 580	GAA CTT Glu AAA TTT Lys	GTA CAT Val 64 ACT TGA Thr	TGT Thr 10 GGC CCG Gly 690	CAA Val GCA CGT Ala	GCT CGA Ala TGG ACC TIP	GAA Leu 550 GAT CTA ASP 70	TTA ASN TCA AGT Ser	GAC CTG Asp AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TTT AGA Ser	ACT TGA Thr ACT TGA Thr	ACT TGA Thr 67 TTA AAT Leu AAA	GTC Glm> 70 ACA TGT Thr> 720
•	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 580 GTT CAA	GAA CTT Glu AAA TTT Lys AAC TTG	GTA CAT Val 64 ACT TGA Thr AGC TCG	TGT Thr 10 GGC CCG Gly 690 AAA TTT	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC TIP	GAA Leu 550 GAT CTA Asp 70 ACA TGT	TTA ASN TCA AGT Ser OO	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr ACT TGA	ACT TGA Thr 67 TTA AAT Leu AAA TTT	GTC Glm> 70 ACA TGT Thr> 720 CAA GTT
	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 580 GTT CAA	GAA CTT Glu AAA TTT Lys AAC TTG	GTA CAT Val 64 ACT TGA Thr AGC TCG	TGT Thr 10 GGC CCG Gly 690 AAA TTT	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC TIP	GAA Leu 550 GAT CTA Asp 70 ACA TGT	TTA ASN TCA AGT Ser OO	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr ACT TGA	ACT TGA Thr 67 TTA AAT Leu AAA TTT	GTC Glm> 70 ACA TGT Thr> 720
•	AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCT Gly AAA TTT Lys 580 GTT CAA Val	GAA CTT Glu AAA TTT Lys AAC TTG	GTA CAT Val 64 ACT TGA Thr AGC TCG	TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT	GCT CGA Ala TGG ACC TIP	GAA Leu 550 GAT CTA Asp 70 ACA TGT	TTA ASN TCA AGT Ser OO	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCT AGA Ser	ACT TGA Thr ACT TGA Thr ACT TGA Thr	ACT TGA Thr 67 TTA AAT Leu AAA TTT	GTC Glm> 70 ACA TGT Thr> 720 CAA GTT
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	CCT Gly AAA TTT Lys 580 GTT CAA Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTA CAT Val 64 ACT TGA Thr AGC TCG Ser	TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys	GCT CGA Ala TGG ACC Trp ACT TGA Thr	GAA Leu 550 GAT CTA ASP 70 ACA TGT Thr	TCA AGT Ser CAA GTT Gln	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTG ASD TCT AGA Ser '10 TTT AAA Phe	ACT TGA Thr ACT TGA Thr ACT TGA Thr	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	GTC Gln>  ACA TGT Thr>  720 CAA GTT Gln>
	AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	CCT Gly AAA TTT Lys 580 GTT CAA Val 73	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTA CAT Val 64 ACT TGA Thr AGC TCG Ser	TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	CAA Val GCA CGT Ala AAA TTT Lys	GCT CGA Ala TGG ACC Trp ACT TGA Thr	GAA Leu 550 GAT CTA ASP 70 ACA TGT Thr	TCA AGT Ser CAA GTT Gln 750	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTG ASN TCT AGA Ser 10 TTT AAA Phe 76	ACT TGA Thr ACT TGA Thr O	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>
	AAA TTT Lys • GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA TGT	CCT Gly AAA TTT Lys 580 GTT CAA Val 7:	GAA CTT Glu AAA TTT Lys AAC TTG ASD	GTA CAT Val 64 ACT TGA Thr AGC TCG Ser GTA CAT	TGT Thr 10 GGC CCG Gly 690 AAA TTT Lys	GCA CGT Ala AAA TTT Lys CAA GTT	GCT CGA Ala TGG ACC Trp ACT TGA Thr	GAA Leu 550 GAT CTA ASP 70 ACA TGT Thr	TCA AGT Ser CAA GTT Gln 750 TCC AGG	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTG CAC Val	TTG ASN TCT AGA Ser 10 TTT AAA Phe 76 ACC TGG	ACT TGA Thr ACT TGA Thr O AAT TTA	ACT TGA Thr 67 TTA AAT Leu AAA TTT Lys	GTC Gln> 70 ACA TGT Thr> 720 CAA GTT Gln>

FIGURE 24 (2 of 3)

B-31 OSP A /PGAU OSP A FUSION

770 780 790 800 810

GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC GCT TTA

CCG TGT CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT TTG CGA AAT

Gly Thr Ala Val Glu Ile Lys Thr Leu Asp Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

FIGURE 24 (3 of 3)

B31/K48 fusion

10 20 ATG AAA AAA TAT TTA TTG GGA ATA GGT CTA ATA TTA GCC TTA ATA GCA TAC TIT TIT ATA AAT AAC CCT TAT CCA GAT TAT AAT CGG AAT TAT CGT Met Lys Lys Tyr Leu Leu Gly Ile Gly Leu Ile Leu Ala Leu Ile Ala> 50 60 70 . 80 TGT AAG CAA AAT GTT AGC AGC CTT GAC GAG AAA AAC AGC GTT TCA GTA ACA TTC GTT TTA CAA TCG TCG GAA CTG CTC TTT TTG TCG CAA AGT CAT Cys Lys Gln Asn Val Ser Ser Leu Asp Glu Lys Asn Ser Val Ser Val> 100 110 120 140 GAT TTG CCT GGT GAA ATG AAA GTT CTT GTA AGC AAA GAA AAA AAC AAA CTA AAC GGA CCA CTT TAC TTT CAA GAA CAT TCG TTT CTT TTT TTG TTT Asp Leu Pro Gly Glu Met Lys Val Leu Val Ser Lys Glu Lys Asn Lys> 150 160 170 180 GAC GGC AAG TAC GAT CTA ATT GCA ACA GTA GAC AAG CTT GAG CTT AAA CTG CCG TTC ATG CTA GAT TAA CGT TGT CAT CTG TTC GAA CTC GAA TTT Asp Gly Lys Tyr Asp Leu Ile Ala Thr Val Asp Lys Leu Glu Leu Lys> 200 210 220 230 GGA ACT TCT GAT AAA AAC AAT GGA TCT GGA GTA CTT GAA GGC GTA AAA CCT TGA AGA CTA TTT TTG TTA CCT AGA CCT CAT GAA CTT CCG CAT TTT Gly Thr Ser Asp Lys Asn Asn Gly Ser Gly Val Leu Glu Gly Val Lys> 250 260 270 . GCT GAC AAA AGT AAA GTA AAA TTA ACA ATT TCT GAC GAT CTA GGT CAA CGA CTG TTT TCA TTT CAT TTT AAT TGT TAA AGA CTG CTA GAT CCA GTT Ala Asp Lys Ser Lys Val Lys Leu Thr Ile Ser Asp Asp Leu Gly Gln> 290 300 310 320 330 ACC ACA CTT GAA GTT TTC AAA GAA GAT GGC AAA ACA CTA GTA TCA AAA TGG TGT GAA CTT CAA AAG TTT CTT CTA CCG TTT TGT GAT CAT AGT TTT Thr Thr Leu Glu Val Phe Lys Glu Asp Gly Lys Thr Leu Val Ser Lys> 340 350 360 370 380 AAA GTA ACT TCC AAA GAC AAG TCA TCA ACA GAA GAA AAA TTC AAT GAA TTT CAT TGA AGG TTT CTG TTC AGT AGT TGT CTT TTT AAG TTA CTT Lys Val Thr Ser Lys Asp Lys Ser Ser Thr Glu Glu Lys Phe Asn Glu> 390 400 410 420 430 AAA GGT GAA GTA TCT GAA AAA ATA ATA ACA AGA GCA GAC GGA ACC AGA TIT CCA CTT CAT AGA CTT TTT TAT TAT TGT TCT CGT CTG CCT TGG TCT Lys Gly Glu Val Ser Glu Lys Ile Ile Thr Arg Ala Asp Gly Thr Arg> FIGURE 25 (1 of 2)

B31/K48 fusion

450 470 480 CTT GAA TAC ACA GGA ATT AAA AGC GAT GGA TCT GGA AAA GCT AAA GAG GAA CTT ATG TGT CCT TAA TTT TCG CTA CCT AGA CCT TTT CGA TTT CTC Leu Glu Tyr Thr Gly Ile Lys Ser Asp Gly Ser Gly Lys Ala Lys Glu> 510 500 520 GTT TTA AAA GGC TAT GTT CTT GAA GGA ACT CTA ACT GCT GAA AAA ACA CAN AAT TIT CCG ATA CAA GAA CIT CCT TGA GAT TGA CGA CIT TIT TGT Val Leu Lys Gly Tyr Val Leu Glu Gly Thr Leu Thr Ala Glu Lys Thr> = :: ; 560 570 530 ACA TTG GTG GTT AAA GAA GGA ACT GTT ACT TTA AGC AAA AAT ATT TCA TGT AAC CAC CAA TTT CTT CCT TGA CAA TGA AAT TCG TTT TTA TAA AGT Thr Leu Val Val Lys Glu Gly Thr Val Thr Leu Ser Lys Asn Ile Ser> 590 600 610 AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser Ala> 630 640 650 660 670 GCT ACT AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA CGA TGA TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT Ala Thr Lys Lys Thr Ala Ala Trp Asn Ser Lys Thr Ser Thr Leu Thr> 690 680 700 710 720 ATT AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC AGA AAA GAA TAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT Ile Ser Val Asn Ser Gln Lys Thr Lys Asn Leu Val Phe Thr Lys Glu> 730 740 750 760 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA GAA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT CTT Asp Thr Ile Thr Val Gln Lys Tyr Asp Ser Ala Gly Thr Asn Leu Glu> 780 800 770 810 GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

FIGURE 25 (2 of 2)

## B-31 OSP A/ 25015 OSP A FUSION

			10			20			30	)			40		•
	. •		•	•		•		•	•	,	•		•	•	•
ATC	AAA S	AAA	TAT	ATT	TIG	GGA	ATA .	GGT	CTA	ATA	TTA	GCC	TT	ATA A	GCA
TAC	TTT	TTT	ATA	AAT	AAC	CCI	TAT	CCA	GAT	TAT	' AAT	CCC	<b>LAA</b>	TAT	CCI
net	Lys	rys	ıyr	Leu	Leu	Gly	Ile	Gly	Leu	Ile	Leu	Ala	Leu	Ile	: Ala>
50			60				70			80			90		•
. •		•	•	-	•		•	•		•		•	•		•
101	AAG	CAA	ተጥአ	CAN	AGC	AGC	CTT	GAC	GAG	AAA	AAC	AGC	CII	TCA	GTA
CVS	Lvs	Gln	Asn	Val	Ser	Ser	T.e.	CIG	Glu	111	TTG	TCG	CAA	AGT	CAT Val>
-, -	_, _			• • •			200	nsp	GIU	LYS	-wan	ser	Val	Ser	Val>
1	00	_	•	110		_	120			1.	30			140	
TAG	<b>عليد</b> -	СС-Д- -	CCT	CAA	እጥር:	222	C-11-42	~~~	~m.	100	•	•		•	
CTA	TTG	GGA	CCA	CTT	TAC	TAT	CYY	CII	CAT	TCG	AAA	GAA	AAA	AAC	AAA
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Ive	CIT	Tyr	TTG	TTT Lys>
	•					•					<b>-</b> 2, 5	010	Lys	ASII	Lys>
	150		_	10	50	_	:	170			180			1	90
C & C	CCC -	AAC	TAC	CAT	Cmy.	y	CC1		C=1	•	•		•		• •
CTG	CCG	TTC	ATG	CTA	CIA	WII	CCT	TCT	CITA	GAC	AAG	CTT	GAG	CII	AAA
Asp	Gly	Lys	Tyr	Asp	Leu	Ile	Ala	Thr.	Val	7 ED	Tye	GAA	CTC	GAA	TTT Lys>
		-	•	•				•••	,	nsp	Dy S	Deu	GIU	Leu	Lys>
	7	200			210			22	20		2	30			240
•				•	*		•								
001									•	•		•		•	•
GGA	ACT	TCT	GAT	AAA	AAC	AAT	GGA	TCT	GGA	GTA	CTT	GAA	GGC	• GTA	AAA
CCT	TGA	AGA	CTA	TTT	TTG	TTA	CCT	AGA	CCT	CAT	GAA	CTT	CCG	CAT	للملحك
CCT	TGA	AGA	CTA	TTT	TTG	TTA	CCT	AGA	CCT	CAT	GAA	CTT	CCG	CAT	AAA TTT Lys>
CCT	TGA	AGA	CTA Asp	TTT	TTG Asn	TTA	CCT	AGA	CCT	CAT	GAA	CTT	CCG	CAT	للملحك
Gly	TGA Thr	AGA Ser 25	CTA Asp	TTT Lys	TTG Asn 2	ASD 60	Gly	AGA Ser	CCT Gly 270	CAT Val	GAA Leu	CTT Glu 28	CCG Gly	CAT Val	TTT Lys>
GCT	TGA Thr	AGA Ser 25	CTA Asp 60 AGT	TTT Lys	TTG Asn 2 GTA	ASD 60	CCT Gly TTA	AGA Ser *	CCT Gly 270	CAT Val	GAA Leu	CTT Glu 28	CCG Gly 0	CAT Val	TTT Lys>
Gly GCT GCT CGA	TGA Thr GAC CTG	AGA Ser 25 AAA TTT	CTA Asp  O AGT TCA	TTT Lys * AAA TTT	TTG Asn 2 GTA CAT	TTA Asn 60 AAA TTT	CCT Gly TTA AAT	AGA Ser * ACA TGT	CCT Gly 270 ATT TAA	CAT Val TCT AGA	GAA Leu • GAC CTG	CTT Glu 28 GAT CTA	CCG Gly 0 • CTA	CAT Val	TTT Lys> CAA
GCT GCT CGA Ala	TGA Thr	AGA Ser 25 AAA TTT	CTA Asp  0 AGT TCA Ser	TTT Lys * AAA TTT	TTG Asn 2 GTA CAT	TTA Asn 60 AAA TTT	CCT Gly TTA AAT	AGA Ser * ACA TGT	CCT Gly 270 ATT TAA	CAT Val TCT AGA	GAA Leu • GAC CTG	CTT Glu 28 GAT CTA	CCG Gly 0 • CTA	CAT Val	TTT Lys> CAA
Gly GCT GCT CGA	TGA Thr GAC CTG	AGA Ser 25 AAA TTT	CTA Asp  O AGT TCA	TTT Lys * AAA TTT	TTG Asn 2 GTA CAT	TTA Asn 60 AAA TTT	CCT Gly TTA AAT Leu	AGA Ser * ACA TGT	CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA	GAA Leu • GAC CTG	CTT Glu 28 GAT CTA Asp	CCG Gly 0 • CTA	CAT Val	TTT Lys> CAA
GCT CGA Ala	TGA Thr • GAC CTG Asp	AGA Ser 25 AAA TTT Lys	AGT TCA Ser	Lys  AAA TTT Lys	TTG Asn 2 GTA CAT Val	ASD ASD AAA TTT Lys	CCT Gly TTA AAT Leu	AGA Ser * ACA TGT Thr	CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA Ser 20	GAA Leu GAC CTG Asp	CTT Glu 28 GAT CTA Asp	CCG Gly O • CTA GAT Leu	CAT Val GGT CCA Gly	TTT Lys> CAA GTT Gln>
GCT CGA Ala 290	TGA Thr GAC CTG Asp	AGA Ser 25 AAA TTT Lys	AGT TCA Ser	Lys  AAA TTT Lys  GTT	TTG Asn 2 GTA CAT Val	AAA TTT Lys 31	CCT Gly TTA AAT Leu 0	AGA Ser ACA TGT Thr	CCT Gly 270 ATT TAA Ile  3	CAT Val TCT AGA Ser 20	GAA Leu GAC CTG Asp	CTT Glu 28 GAT CTA Asp	CCG Gly O CTA GAT Leu 330	CAT Val GGT CCA Gly	TTT Lys> CAA GTT Gln>
GCT CGA Ala 290 ACC TGG	TGA Thr GAC CTG Asp	AGA Ser 25 AAA TTT Lys CTT GAA	ASP  AGT TCA Ser  300  GAA CTT	Lys AAA TTT Lys GTT CAA	TTG Asn 2 GTA CAT Val TTC AAG	AAA TTT AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 0 GAA	AGA Ser ACA TGT Thr	CCT Gly 270 ATT TAA Ile  3	CAT Val TCT AGA Ser 20	GAA Leu GAC CTG ASP	CTT Glu 28 GAT CTA Asp	CCG Gly O CTA GAT Leu 330	CAT Val GGT CCA Gly	TTT Lys> CAA GTT Gln> AAA
GCT CGA Ala 290 ACC TGG	TGA Thr GAC CTG Asp	AGA Ser 25 AAA TTT Lys CTT GAA	ASP  AGT TCA Ser  300  GAA CTT	Lys AAA TTT Lys GTT CAA	TTG Asn 2 GTA CAT Val TTC AAG	AAA TTT AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 0 GAA	AGA Ser ACA TGT Thr	CCT Gly 270 ATT TAA Ile  3	CAT Val TCT AGA Ser 20	GAA Leu GAC CTG ASP	CTT Glu 28 GAT CTA Asp	CCG Gly O CTA GAT Leu 330	CAT Val GGT CCA Gly	TTT Lys> CAA GTT Gln>
GCT CGA Ala 290 ACC TGG	TGA Thr GAC CTG Asp ACA TGT Thr	AGA Ser 25 AAA TTT Lys CTT GAA	ASP  AGT TCA Ser  GAA CTT Glu	Lys AAA TTT Lys GTT CAA	TTG Asn 2 GTA CAT Val TTC AAG	AAA TTT AAA TTT AAA TTT AAA TTT	CCT Gly TTA AAT Leu 0 GAA	AGA Ser ACA TGT Thr	CCT Gly 270 ATT TAA Ile  3	CAT Val TCT AGA Ser 20	GAA Leu GAC CTG ASP ACA	CTT Glu 28 GAT CTA Asp	CCG Gly 0 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly	TTT Lys> CAA GTT Gln> AAA
GCT CGA Ala 290 ACC TGG Thr	TGA Thr GAC CTG Asp ACA TGT Thr	AGA Ser 25 AAA TTT Lys CTT GAA Leu	ASP  AGT TCA Ser  GAA CTT Glu	Lys AAA TTT Lys GTT CAA Val	TTG Asn 2 GTA CAT Val TTC AAG Phe	AAA TIT Lys AAA TIT Lys	CCT Gly TTA AAT Leu O GAA CTT Glu 360	AGA Ser ACA TGT Thr GAT CTA Asp	CCT Gly 270 ATT TAA Ile  3 GGC CCG Gly	TCT AGA Ser 20 AAA TTT Lys	GAA Leu GAC CTG Asp ACA TGT	CTT Glu 28 GAT CTA Asp CTA GAT Leu	CCG Gly 0 * CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser	CAA GTT Gln> AAA TTT Lys>
GCT CGA Ala 290 ACC TGG Thr	GAC CTG ASP ACA TGT Thr	AGA Ser 25 AAA TTT Lys CTT GAA Leu	ASP  AGT TCA Ser  GAA CTT Glu  TCC	AAA TTT Lys GTT CAA Val 50 AAA	TTG Asn 2 GTA CAT Val TTC AAG Phe	AAA TIT Lys AAA TIT Lys AAA TAT AAA TAT AAA TAT AAA TAT AAA TAT AAA	CCT Gly TTA AAT Leu 0 GAA CTT Glu 360	AGA Ser ACA TGT Thr GAT CTA Asp	CCT Gly 270 ATT TAA Ile  3 GGC CCG Gly	TCT AGA Ser 20 AAA TTT Lys	GAA Leu GAC CTG Asp ACA TGT	CTT Glu 28 GAT CTA Asp CTA GAT Leu	CCG Gly 0 * CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser BO	CAA GTT Gln> AAA TTT Lys>
GCT CGA Ala 290 ACC TGG Thr	TGA Thr GAC CTG Asp ACA TGT Thr	AGA Ser 25 AAA TTT Lys CTT GAA Leu ACT	ASP  AGT TCA Ser  GAA CTT Glu  TCC AGG	Lys  AAA TTT Lys  GTT CAA Val 50 AAA TTT	TTG ASN 2 GTA CAT Val TTC AAG Phe GAC CTG	AAA TTT Lys AAA TTT Lys AAA TTT AAA TTT Lys	TTA AAT Leu  GAA CTT Glu  360 TCA AGT	AGA Ser * ACA TGT Thr GAT CTA Asp	CCT Gly 270 ATT TAA Ile  3 GGC CCG Gly ACA	TCT AGA Ser 20 AAA TTT Lys 37	GAA Leu GAC CTG ASP ACA TGT	CTT Glu 28 GAT CTA Asp CTA GAT Leu AAA	CCG Gly  CTA GAT Leu  330 GTA CAT Val  3	GGT CCA Gly TCA AGT Ser 80	CAA GTT Gln> AAA TTT Lys>

FIGURE 26 (1 of 3)

#### B-31 OSP A/ 25015 OSP A FUSION

	390			4 (	00			410			420	-		4	30
* * * * * * * * * * * * * * * * * * * *	GGT.	CAA	GTA	ጥርጥ	Cy y	* * * * * * * * * * * * * * * * * * * *	እጥአ	# አጥአ	3 C 3	* >C>	•	C2C	•		• AGA
															TCT
															Arg>
		140			450				60			470			400
•	7	*		•	*		•	•	•	•		* 70		•	480 •
											GGA				
GAA	CTT	ATG	TGT	CCT	TAA	TTT	TCG	CTA	CCT	AGA	CCT	TTT	CGA	TIT	CTC Glu>
Deu	014	-3-		013		Ly 5	261	rap	GIY	261	GIY	Lys	WIG	Lys	C1n>
		45	90	_	5	500		_	510			5	20		
GTT	TŤA	AAA	GGC	TAT	GTT	CTT	GAA	CCA	₽ ₽	<b>CTA</b>	ACT	CCT	e Gaa	ድ አ አ	202
											TGA				
·Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530			540			50	50			560			570		
•		•	*		•	-	*	•	•	•		•	•		•
ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT	TCA
TGT	Leu	'Val	CAA Val	LVS	Glu	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAA	AGT Ser>
				-2-			****		1111	Dea	261	Lys	W211	775	Sers
					•										•
58	30	_	5	590	•	_	600			61	.0		6	520	•
	•	GGG		•	TCA	• GTT	•	CTT	• AAT		•	•		•	CCT
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	ATT	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	ATT	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	GCT CGA Ala>
AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	ATT	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGA Ala>
AAA TTT Lys	TCT AGA Ser 630	G1A CCC	GAA CTT Glu	GTT CAA Val	AGT Ser	CAA Val	GAA CTT Glu	GAA Leu 50	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu	GTT CAA Val 64	AGT Ser 10 • GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 550	TTA Asn GCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA	TTA Asn GCA CGT	GAC CTG Asp	ACT TGA Thr 660 ACT	CTG Asp TCA AGT	AGT TCA Ser • ACT	AGT TCA Ser 67	CGA Ala> C ACA TGT
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 GCA CGT Ala	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA Asn	TTA Asn GCA CGT Ala	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCA AGT Ser	AGT TCA Ser • ACT	AGT TCA Ser 67	CGA Ala> C ACA TGT Thr>
AAA TTT Lys GCT CGA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 AAT TTA	TTA Asn GCA CGT Ala	GAC CTG Asp	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCA AGT	AGT TCA Ser • ACT	AGT TCA Ser 67	CGA Ala> C ACA TGT
AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 580 •	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASD 70	GCA CGT Ala	GAC CTG Asp * GGC CCG Gly	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> CCA ACA TGT Thr> 720 CAA
AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680 GTA CAT	GAA CTT Glu AAA TTT Lys AAC TTG	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASN 70	GCA CGT Ala 00 GCC CGG	GAC CTG Asp • GGC CCG Gly CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser '10	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> CCA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680 GTA CAT	GAA CTT Glu AAA TTT Lys AAC TTG	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASN 70	GCA CGT Ala 00 GCC CGG	GAC CTG Asp • GGC CCG Gly CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser '10	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> CCA ACA TGT Thr> 720 CAA
AAA TTT Lys GCT CGA Ala ATT TAA	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 80 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG	GTT CAA Val 64 ACT TGA Thr AAC TTG	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC TIP	GAA Leu 550 AAT TTA ASN 70	GCA CGT Ala 00 GCC CGG	GAC CTG Asp • GGC CCG Gly CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCA AGT Ser '10	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala> CCA TGT Thr> 720 CAA GTT
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 80 GTA CAT Val	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750	GAC CTG Asp GGC CCG Gly CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 10 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala>  ACA TGT Thr>  720  CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 880 GTA CAT Val 7:	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG Asn TCA	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala 00 GCC CGG Ala 750 TCA	GAC CTG Asp GGC CCG Gly CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 10 TTT AAA Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala>  ACA TGT Thr>  720  CAA GTT Gln>
AAA TTT Lys GCT CGA Ala ATT TAA Ile GAC CTG	TCT AGA Ser 630 ACT TGA Thr ACT TGA Thr	CCC Gly AAA TTT Lys 580 GTA CAT Val 7:	GAA CTT Glu AAA TTT Lys AAC TTG Asn	GTT CAA Val 64 ACT TGA Thr AAC TTG ASn TCA AGT	AGT Ser 10 GCA CGT Ala 690 AAA TTT Lys CAA GTT	CAA Val GCT CGA Ala AAA TTT Lys AAA TTT	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 70 AAA TTT Lys	GCA CGT Ala OCC CGG Ala 750 TCA AGT	GAC CTG Asp GGC CCG Gly CTT GAA Leu GCA CGT	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCA AGT Ser 10 * TTT AAA Phe 76	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala>  ACA TGT Thr>  720  CAA GTT Gln>

FIGURE 26 (2 of 3)

49//33

## B-31 OSP A/ 25015 OSP A FUSION

770			780			79	90			800	•		810		
•		•	•		•		•	•		•		•	•		•
					ATT										
CCG	TGT	CGT	CAG	CTT	TAA	TTT	TGT	GAA	CTA	CTT	GAA	TTT	TIG	CGA	TAA
Gly	Thr	Ala	Val	Glu	Ile	Lys	Thr	Leu	Asp	Glu	Leu	Lys	Asn	Ala	Leu>
					•					· <b>-</b>				•	

AGA TCT Arg>

FIGURE 26 (3 of 3)

#### K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

10	20	30	40	
*	•	• •	•	•
ATG AAA AAA TAT TI	TA TTG GGA ATA	GGT CTA ATA	TTA GCC TTA	ATA GCA
TAC TTT TTT ATA AA	AT AAC CCT TAT	CCA GAT TAT	AAT CGG AAT	TAT CGT
Met Lys Lys Tyr Le	eu Leu Gly Ile	Gly Leu Ile	Leu Ala Leu	Ile Ala>
	•			
50 60	70 .	. 80	90	
• •	• •	• •	•	•
TGT AAG CAA AAT GT	IT AGC AGC CT	CAT GAA AÀA	AAT AGC GTT	TCA GTA
ACA TTC GTT TTA CA	aa tcg tcg gai	CTA CTT TITE	TTA TCG CAA	AGT CAT .
Cys Lys Gln Asn Va	al Ser Ser Le	Asp Glu Lys	Asn Ser Val	Ser Val>
_				
100 110	0 120	13	0 1	140
• •	•		* *	•
GAT TTA CCT GGT GG	GA ATG ACA GT	CTT GTA AGT	AAA GAA AAA	GAC AAA
CTA AAT GGA CCA CC	CT TAC TGT CA	A GAA CAT TCA	THE CIT THE	CTG TTT
Asp Leu Pro Gly G	ly Met Thr Va.	I Leu val Ser	ras cia ras	Asp Lys>
	1.60	170	180	190
150	160	* *	* *	150
GAC GGT AAA TAC AG	כיד כידו האה הר	ACA GTA GAC	AAG CTT GAG	CTT AAA
CTG CCA TTT ATG TO	CA GAT CTC CG	T TGT CAT CTG	TTC GAA CTC	GAA TTT
Asp Gly Lys Tyr S	er Leu Glu Al	Thr Val Asp	Lys Leu Glu	Leu Lys>
Asp GI D/S 1/1 D			-	-
200	210	220	230	240
• •	• •	• •	•	• •
GGA ACT TCT GAT A	AA AAC AAC GG	T TCT GGA ACA	CTT GAA GGT	GAA AAA
CCT TGA AGA CTA T	TT TIG TIG CC	A AGA CCT TGT	GAA CTT CCA	CIT III
Gly Thr Ser Asp L	ys Asn Asn Gl	y Ser Gly Thr	Leu Glu Gly	Glu Lys>
250	260	270	280	
ACT GAC AAA AGT A		א ארא אידער כולידי י	באת האת כתא	ACT CAA
TGA CTG TTT TCA T	MA GIA AAA II	T TOT TAA COA	CTA CTG GAT	TCA GTT
Thr Asp Lys Ser L	us Val III An	u Thr Ile Ala	Asp Asp Leu	Ser Gln>
The Asp Dys Set D	Jys var bys bo			
290 300	310	320	330	
* * *	• •	• •	• •	•
ACT AAA TTT GAA A	ATT TTC AAA GA	A GAT GCC AAA	ACA TTA GTA	TCA AAA
TGA TTT AAA CTT T	TAA AAG TTT CI	T CTA CGG TTT	TGT AAT CAT	AGT TTT
Thr Lys Phe Glu	Ile Phe Lys Gl	u Asp Ala Lys	Thr Leu Val	Ser Lys>
			· 	
340 35	50 36	30 3	70	380
•	•	• •	* *	•
AAA GTA ACC CTT	AAA GAC AAG T	TA TOA ACA GAA	GAA AAA TTC	AAC GAA
TTT CAT TGG GAA	TTT CTG TTC A	FT AGT TGT CTT	CIT TIT AAG	, TIG CII
Lys Val Thr Leu	LYS ASD LYS S	st set int Gin	. Giu Lys Phe	: Wan GIOS

FIGURE 27 (1 of 3)

### K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

		390			40	0		.4	10		•	420		•	43	0
	• AAG	GGT	GAA	ACA	TCT	GAA	AAA	ACA	ATA	GTA	AGA	GCA	TAA	GGA	ACC	AGA
	$\tau\tau$	CCA	CTT	TGT	AGA	CTT	TTT	TGT	TAT	CAT	TCT	CGT	ATT	CCT	TGG	TCT
	Lys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
•		4	140		•	450		_	46	0	_	4	70		_	480
	•		TAC		•	<b>.</b>		» CC	CAT	GG»	TCC -	CCA	222	CCT	444	G2 A
	CTT	GAA	ATG	TCT	CTC	TAT	ጥጥ	TCG.	CTA	CCT	AGG.	CCT	TTT	CGA	TTT	CII
	Leu	Glu	TVI	Thr	Asp	Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys	Gluż
	-		49				00			510			52	•		
		•		•	•		•		•	•		•		•		
•	GTT	TTA	AAA	GAC	TTT	ACT	CTT	GAA	GGA	ACT	CTA	GCT	GCT	GAC	GGC	AAA
	CAA	AAT	TTT	CTG	AAA	TGA	GAA	Glu	GLY	Thr	Leu	Ala	Ala	ASD	Glv	Lys>
	Val	Leu	Lys	Asp	Pne	1111	Dea	Giu	Giy	* * * * *	200				0-3	<b>_</b>
	530		-	540			55	50		5	560		•	570		
	•		•	•		•		•	•		•		• .	•		-
	ACA	ACA	TTG AÁC	AAA	GTT	ACA	GAA	GGC	ACT	GTT	GTT	TTA	AGC	AAG	ATT	ACT
à,	TGT	TGT	AAC	TTT	CAA	Thr	Glu	CCG	Thr	Val	Val	Leu	Ser	Lvs	Ile	Ser>
	Tur	Ini	Leu	ry 2	VOI	1 1 1 1 1	010	023								
	5	80		;	590			600			6:	10		•	520	
		•	•		•		•	•		*		.•	•		•	
.2.	AAA	· TCT	GGG	GAA	GTT	TCA	GTT	GAA	TTO	* AAT	GAC	 ACT	GAC CTG	AGT	AGT	GCT CGA
-2.	<b>AAA</b> TTT	TCT	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
-2.	<b>AAA</b> TTT	TCT	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	GCT CGA Ala>
-a.	<b>AAA</b> TTT	TCT	Gly	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA Ser	CGA
-2.	AAA TTT Lys	TCT AGA Ser	ccc Gly	GAA CTT Glu	GTT CAA Val	AGT Ser 40	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
-2. 	AAA TTT Lys	TCT AGA Ser 630	CCC Gly	GAA CTT Glu	GTT CAA Val 6	AGT Ser 40 • GCA	CAA Val	GAA CTT Glu	GAA Leu 650 AAT	TTA ASD TCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala> 70 * ACA
-2. -2.	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA	TTA ASD TCA AGT	GAC CTG ASP * AAA TTT	ACT TGA Thr 660 ACT TGA	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT
enter de la companya	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 GCA CGT Ala	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA Asn	TTA ASD TCA AGT Ser	GAC CTG ASP * AAA TTT	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT Thr>
-2.	AAA TTT Lys GCT	TCT AGA Ser 630	CCC Gly AAA	GAA CTT Glu AAA	GTT CAA Val 6 ACT TGA	AGT Ser 40 • GCA CGT	CAA Val GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 650 AAT TTA Asn	TTA ASD TCA AGT	GAC CTG ASP * AAA TTT	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> 70 ACA TGT
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA	CCC Gly	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40  GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC TIP	GAA Leu 650 AAT TTA Asn	TTA ASD TCA AGT Ser	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thi	CCC Gly	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	TTA ASD TCA AGT Ser	GAC CTG ASP AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
-2.	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	TTA ASD TCA AGT Ser 00 AAC	GAC CTG ASP AAA TIT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr>
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 CAC CAC	GAA CTT Glu AAA TTT Lys AAT	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	TTA ASD TCA AGT Ser 00 AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
	AAA TTT Lys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 CAC CAC	GAA CTT Glu AAA TTT Lys	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	TTA ASD TCA AGT Ser 00 AAC	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT
	AAA TTT Lys GCT CGA Ala ATT	TCT AGA Ser 630 ACT TGA Thi	CCC Gly AAA TTT Lys 680 CACAC CAC	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr	AGT Ser 40 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG	GAA Leu 650 AAT TTA ASD 7 AAA TTT Lys	TTA ASD TCA AGT Ser 00 AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
era.	AAA TTT Lys GCT CGA Ala ATI TAA Ile	TCT AGA Ser 630 ACT TGA Thi CAGC Ser CACC	CCC Gly Gly AAA TTT Lys 680 CGG CAC CAC TAT TAT	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr CAG Ser	AGT Ser  40 GCA CGT Ala 690 CAA GTT CAA	CAA Val GCT CGA Ala AAA TTT Lys 740	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 650 AAT TTA Asn 7 AAA TTT Lys	TTA ASD TCA AGT Ser 00 AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser 710 TTC AAG Phe 7	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>
erania	AAA TTT Lys GCT CGA Ala ATI TAA Ile	TCT AGA Ser 630 ACT TGA Thi CAGC Ser CACC	CCC Gly Gly AAA TTT Lys 680 CGG CAC CAC TAT TAT	GAA CTT Glu AAA TTT Lys AAT TTA AST	GTT CAA Val 6 ACT TGA Thr CAG Ser	AGT Ser  40 GCA CGT Ala 690 CAA GTT CAA	CAA Val GCT CGA Ala AAA TTT Lys 740	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 650 AAT TTA Asn 7 AAA TTT Lys	TTA ASD TCA AGT Ser 00 AAC TTG ASD	GAC CTG ASP AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser 710 TTC AAG Phe 7	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala> 70 ACA TGT Thr> 720 GAA CTT Glu>

FIGURE 27 (2 of 3)

K48 OSP A / B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA
CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT
Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

FIGURE 27 (3 of 3)

## B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

			10			20			3	0			40		
	•		•	•	•	•		•	-	•	•	•	•		•
ATO	G AA	A AA	A TAT	TT7	TTC	GGZ	ATA	A GG	T CT	'A AT	A TT	A GC	TT.	A AT	A GCA
134	- 11.	1 11	L ATA	AA'	i. AAC	: CC7	TAT	ר ככ	A GA	ፐ ጥል	יממ די	T CC(		T	
Met	L Ly:	s Ly:	s iyi	Let	Leu	Gly	, Ile	e Gl	y Le	u Il	e Le	ı Ala	a Le	u Il	e Ala:
50			60	)			70			80			91	D	
		•	•		•		•		• .	•		•	•	r	•
101	1 AA(	CA	LAA!	GII	, AGC	AGC	CTI	GA:	r GA	A AA	A AAT	AGC	GT	גסד ז	GTA
CVS	Lvs	Gli	Asn	Val	 	Ser	GAA	L CTZ	CI	ran	r- Tirk	TCG	CA	A AG	CAT
-, -						361	Dec	. ASI	) GI	u Ly:	S AST	Ser	· Val	Ser	CAT Val>
1	.00			110			120	)		;	130			140	
	•	-		•		•	•		•		•	•		_	•
CTA	מניני :	CCI	GGT	GGA	ATG	ACA	GTT	CTI	GT	A AG	AAA 1	GAA	AAA .	GAC	AAA
Asp	Leu	Pro	Gly	CLI	MAC	The	CAA	GAA	CAT	TCA	TTT	, CLL	TTI	CTG	TTT
			, 01,	Q <sub>2</sub> y	1166	1311	A91	Leu	va.	l Sei	Lys	Glu	Lys	Asp	Lys>
•	150			1	60			170			180			1	90
*	•		•		•	•		•		•	•		•		_
CTC	GGT	AAA TTT	TAC	AGT	CTA	GAG	GCA	ACA	. GTA	GAC	AAG	CTT	GAG	CTT	AAA
Asp	Glv	TNS	TVE	Ser	CAT	CTC	CGT	TGT	CAT	, CIG	TTC	GAA	CTC	GAA	AAA TTT
	<b>-</b> -,	٠,٠	-1-	J-2-2	Deu	GIU	WIG	Int	Val	Asp	Lys	Leu	Glu	Leu	TTT Lys>
:		200			210	•		2	20			230			240
CCN	3 CT	T-T		•	*		•		•	•		•		•	_
CCT	TGA	101	CTA	AAA	TTC	AAC	GGT	TCT	GGA	ACA	CTT	GAA	GGT	GAA	AAA
Gly	Thr	Ser	Asp	Lvs	Asn	ASD	Glv	AGA	CCT	TGT	GAA	CIT	CCA	CTT	TTT Lys>
_	•			_, _			Cly	361	, GIŞ	III	Leu	GIU	Gly	Glu	Lys>
•		2	50		2	60			270			2.8	30 <sup>^</sup>		
ACT	GAC	AAA	AGT	מממ	GT h	***	тт х		*		•		•	•	
TGA	CTG	TTT	TCA	TTT	CAT	TATE	TIM	TCT	ATT.	GCT	GAT CTA	GAC	CTA	AGT	CAA
Thr	Asp	Lys	Ser	Lys	Val	Lys	Leu	Thr	Ile	Ala	Asp	A CTG	GAT	TCA	GTT
						-					nsp	vəb	reu	ser	GID>
290		•	300			31	0		:	320			330		
ACT	AAA	TATE	440	<u>አ</u> ጥጥ	<u>ተ</u> ሞር	222	- 	~		•	ACA	*	•		•
TGA	TTT	AAA	CTT	TAA	AAG	TTT	CTT	CTA	CGG	AAA	ACA TGT	TTA	GTA	TCA	AAA
Thr	Lys	Phe	Glu	Ile	Phe	Lys	Glu	Asp	Ala	Lvs	Thr	LAU	CAT	AGT	TTT
						_		•		-, 0	••••	Dea	AGI	ser	Lys>
34	+	•	3	50		•	360			37	70		3	80	
AAA	GTA	ACC	CTT	AAA	GAC	אמר	ጥር አ	ጥር እ	202	<b></b>	GAA	•		•	
4, 4, 4	C-V 7	100	CMM	111	CIG	TTC .	AGT	ACT	ست		CAL	TV-TV-TO			
Lys	Val	Thr	Leu	Lys	Asp	Lys	Ser	Ser	Thr	G3 11	Glu	TIT .	AAG	TTG	CTT
				-	•	•					Jiu	⊌y S	rne	ASD	<b>GTU&gt;</b>

FIGURE 28 (1 of 3)

# 54/133 B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

٠		390			40	00			410			420			4	30 .
. •	•	•		•		*	•		. •	•	•	•		•		•
																AGA
																TCT
I	Jys	Gly	Glu	Thr	Ser	Glu	Lys	Thr	Ile	Val	Arg	Ala	Asn	Gly	Thr	Arg>
			_		_											
	٠_	4	140		_	450.		_	4 (	50	_	4	170			480
,	~~~	CNA	- mac	101	- -	•			C1 m	-	 	~~`	•		•	•
											TCC					
•	277	Glu	410	101	7.0	TIA	Tare	200	CIM	CCI	AGG	<u>たしょ</u>	111	CGA	1.1.1.	Glu>
1	Jeu	GIU	171	1411	veb	116	Lys	361	ASP	GIY	Ser	GIY	Lys	Ala	Lys	GIU>
			49	90		5	500			510			52	20		
		•		•	*		•		•	*		•		•	•	
											CTA					
(	AA	AAT	TTT	CTG	AAA	TGA	GAA	CIT	CCT	TGA	GAT	CGA	CGA	CTG	CCG	TTT
7	/al	Leu	Lys	Asp	Phe	Thr	Leu	Glu	Gly	Thr	Leu	Ala	Ala	Asp	Gly	Lys>
53	30	•	_	540			5:	50		:	560			570		
_	•							•			•		•	•		•
											GTT					
7	rgt	TGT	AAC	TTT	CAA	TGT	CTT	CCG	TGA	CAA	CAA	AAT	TCG	TTC	TAA	AGT
'1	ınr	Thr	reu	Lys	Val	Thr	GIU	GIA	Thr	Val	Val	Leu	Ser	Lys	Ile	Ser>
	58	30		9	590			600			61	.0		ę	520	
	58	80	•	5	90		•	600		•	61	.0	•	6	20	
,		•	GGG		•	TCA	GTT	•	CTT	+ AAT		•	GAC		•	GCT
	AA	* TCT		GAA	• GTT			GAA			GAC CTG	• ACT		AGT	• AGT	
7	AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA	AGT	CAA	GAA CTT	GAA	TTA	GAC CTG	• ACT TGA	CTG	AGT TCA	AGT TCA	
7	AAA TTT	* TCT AGA Ser	CCC	GAA CTT	GTT CAA Val	AGT Ser	CAA	GAA CTT Glu	GAA Leu	TTA	GAC CTG	ACT TGA Thr	CTG	AGT TCA	AGT TCA Ser	CGA Ala>
7	AAA TTT	• TCT AGA	CCC	GAA CTT	GTT CAA Val	AGT	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	• ACT TGA	CTG	AGT TCA	AGT TCA	CGA Ala>
I	laa TTT Jys	TCT AGA Ser 630	Gly	GAA CTT Glu	GTT CAA Val	AGT Ser	CAA Val	GAA CTT Glu	GAA Leu 550	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
1	AAA TTT .ys	TCT AGA Ser 630 ACT	CCC	GAA CTT Glu	GTT CAA Val 64	AGT Ser 10 • GCA	CAA Val	GAA CTT Glu TGG	GAA Leu 550 *	TTA Asn TCA	GAC CTG Asp	ACT TGA Thr 660	CTG Asp	AGT TCA Ser	AGT TCA Ser 67	CGA Ala> O
1	AAA TTT Jys GCT	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA	TTA Asn TCA AGT	GAC CTG Asp • AAA TTT	ACT TGA Thr 660 ACT TGA	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala>  O ACA TGT
1	AAA TTT Jys GCT	TCT AGA Ser 630 ACT TGA	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA	TTA Asn TCA AGT	GAC CTG Asp	ACT TGA Thr 660 ACT TGA	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala>  O ACA TGT
1	AAA TTT Jys GCT	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA Asn	TTA Asn TCA AGT	GAC CTG Asp • AAA TTT	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala>  O ACA TGT Thr>
1	AAA TTT Jys GCT	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys	GAA CTT Glu AAA TTT	GTT CAA Val 64 ACT TGA	AGT Ser 10 • GCA CGT Ala	CAA Val • GCT CGA	GAA CTT Glu TGG ACC	GAA Leu 550 * AAT TTA Asn	TTA Asn TCA AGT Ser	GAC CTG Asp • AAA TTT	ACT TGA Thr 660 ACT TGA Thr	CTG Asp TCC AGG Ser	AGT TCA Ser ACT TGA	AGT TCA Ser 67 TTA AAT	CGA Ala> O ACA TGT
	AA TTT -ys GCT GGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 •	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr	AGT Ser 10 GCA CGT Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 550 * AAT TTA ASD 70	TCA AGT Ser	GAC CTG Asp • AAA TTT Lys	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu	CGA Ala>  O ACA TGT Thr>  720 GAA
	AAA TTT Jys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680 GTG CAC	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 CAA GTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 * AAT TTA ASD 70 AAA TTT	TTA ASN TCA AGT Ser 00 AAC TTG	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  O ACA TGT Thr>  720 GAA CTT
	AAA TTT Jys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	AAA TTT Lys 680 GTG CAC	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 CAA GTT	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 * AAT TTA ASD 70 AAA TTT	TTA ASN TCA AGT Ser 00 AAC TTG	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  O ACA TGT Thr>  720 GAA
	AAA TTT Jys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA ASD	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp	GAA Leu 550 * AAT TTA ASD 70 AAA TTT	TCA AGT Ser O AAC TTG Asn	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  O ACA TGT Thr>  720 GAA CTT
	AAA TTT Jys GCT CGA Ala	TCT AGA Ser 630 ACT TGA Thr	CCC Gly AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys	GTT CAA Val 64 ACT TGA Thr AGC TCG	AGT Ser 10 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT	GAA CTT Glu TGG ACC Trp	GAA Leu 550 * AAT TTA ASD 70 AAA TTT	TTA ASN TCA AGT Ser 00 AAC TTG	GAC CTG Asp AAA TTT Lys CTT GAA	ACT TGA Thr 660 ACT TGA Thr	TCC AGG Ser	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT	CGA Ala>  O ACA TGT Thr>  720 GAA CTT
	AAA TTT Lys GCT CGA ATT TAA	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser	AAA TTT Lys 680 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA Asn	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser	AGT Ser 10 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 * AAT TTA ASD 70 AAA TTT Lys	TCA AGT Ser O. AAC TTG Asn 750	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys	CGA Ala>  0 ACA TGT Thr> 720 GAA CTT Glu>
	AAA TTT Jys GCT GGA ATT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA	CCC Gly AAA TTT Lys 580 GTG CAC Val	GAA CTT Glu AAA TTT Lys AAT TTA ASN	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser GTA	AGT Ser 10 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 550 *AAT TTA ASD 70 AAA TTT Lys	TTA ASN TCA AGT Ser O AAC TTG ASN 750 TCA	GAC CTG Asp AAA TTT Lys CTT GAA Leu	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe 76	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTY Lys	CGA Ala>  0 ACA TGT Thr>  720 GAA CTT Glu>
	AAA TTT Lys GCT GGA ALTT TAA Ile	TCT AGA Ser 630 ACT TGA Thr AGT TCA Ser ACA TGT	CCC Gly AAA TTT Lys 580 CAC Val 77	GAA CTT Glu AAA TTT Lys AAT TTA Asn 30	GTT CAA Val 64 ACT TGA Thr AGC TCG Ser GTA CAT	AGT Ser 10 GCA CGT Ala 690 CAA GTT Gln	CAA Val GCT CGA Ala AAA TTT Lys AAA TTT	GAA CTT Glu TGG ACC Trp ACC TGG Thr	GAA Leu 50 *AAT TTA ASD 70 AAA TTT Lys GAC CTG	TCA AGT Ser O. AAC TTG Asn 750 TCA AGT	GAC CTG Asp AAA TTT Lys CTT GAA Leu GCA CGT	ACT TGA Thr 660 ACT TGA Thr GTA CAT Val	TCC AGG Ser TTC AAG Phe ACC TGG	AGT TCA Ser ACT TGA Thr ACA TGT Thr	AGT TCA Ser 67 TTA AAT Leu AAA TTT Lys CTA GAT	CGA Ala>  0 ACA TGT Thr>  720 GAA CTT Glu>

FIGURE 28 (2 of 3)

## B-31 OSP A/K48 OSP A/ B-31 OSP A/ K48 OSP A FUSION

770 780 790 800 810

GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC GCT TTA

CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG CGA AAT

Gly Lys Ala Val Glu Ile Thr Thr Leu Lys Glu Leu Lys Asn Ala Leu>

820
AAA TAA
TTT ATT
Lys \*\*\*>

FIGURE 28 (3 of 3)

#### B-31 OSPA/ B-31 OSPB FUSION

	1	0			20			30			4	40			
•	•		•	, <b>•</b>		•		*	•		•		•		
ATG A	AA .	AAA	TAT	TTA	TTG	GGA	ATA	GGT	CTA	ATA	TTA	GCC	TTA	ATA	GCA
TAC T	TT '	TTT	ATA	TAA	AAC	CCT	TAT	CCA	GAT	TAT	AAI.	2 T a	TAN	TAL	Zlas
Met Ly	ys	Lys	Tyr	Leu	Leu	GIA	Tie	GIY	ren	116	Deu.	YIG	Deu	110	7107
50			60			7	70			80			90		
•		•	•		•	•	•	•		*		•	. •		•
TGT A	AG	CAA	AAT	GTT	AGC	AGC	CIT	GAC	GAG	AAA	AAC	AGC	GTT	TCA	GTA
ACA T	TC	GTT	TTA	CAA	TCG	TCG	GAA	CTG	CTC	Tara	7110	106	UAA Ual	AG1	UAI
Cys L	ys	Gln	Asn	Val	Ser	Ser	Leu	ASP	GIU	Lys	WSII	Ser	AGT	SEI	Val
100				110			120			13	30		1	140	
•		•		•		*	•		*		•	*		•	
GAT T	TG	CCT	GGT	GAA	ATG	AAA	GTT.	CII	GTA	AGC	AAA	GAA	AAA	AAC	AAA
CTA A	<b>LAC</b>	GGA	CCA	CTT	TAC	TTT	CAA	GAA	CAT	TCG	TIT	CIT	Tarr	116	THE
Asp L	.eu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser	Lys	GIU	Lys	ASII	Lys>
1	50			1	60		•	170			180			19	0
•	•		•		•	•		•		•	•		•		•
GAC G	GC.	AAG	TAC	GAT	CTA	TTA	GCA	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
CTG	CCG	TTC	ATG	CTA	GAT	TAA	CGT	TGT	CAT	CIG	TIC	GAA	CTC	GAA	TTT
Asp C	Sly	Lys	Tyr	Asp	Leu	Ile	Ala	Thr	Val	Asp	Lys	Leu	GIU	Leu	Lys>
		200			210			2	20			230			240
•		• .		•	•		•		•	•				•	•
GGA A	ACT	TCT	GAT	YYY	AAC	TAA	GGA	TCT	GGA	GTA	CTT	GAA	GGC	GTA	AAA
CCT	TGA	AGA	CTA	TTI	, IIG	TTA	CCT	AGA	CCI	CAT	GAA	CIT	CLG	VAI	125
Gly 1	Thr	Ser	Asp	Lys	AST	AST	GIA	Ser	GIY	AGT	Leu	614	Gry	V-0.1	Lys>
		2	250			260			270	)		2	80		
	•		•	•	•	*		*	•		•		•		
GCT	GAC	<b>LAA</b>	A AG	IAA 1	(GT)	AAA A	ATT .	ACA	TTA A	TCI	GAC	GAT	CIA	GGT	CAA
CGA	CIG	TTI	r TC	4 III	CA?	r TTI	AAI	TG1	TAP	A AGA	. 010	CIM	TAN	CCA	Gln>
Ala .	Asp	Lys	s Se	r Lys	s va.	LLYS	Let	1 1111	. 116	: 561	vsř	, waf	Dea	G L J	Gln>
290			301	0			310			320			330	ì	
•		•		• -	•		•	•	•	•		*	•		•
ACC	AC	CT	T GA	A GT	TTC	C AA	A GAZ	A GA	r GG(	C AA	A AC	CTA	GTA	TCA	AAA
TGG	TGT	r GA	A CT	T CA	A AA	3 TT	rcm	CT	A CCC	3 TT	TGT	r GAT	CAT	AGI	TIT
Thr	Thi	r Le	u Gl	u Vai	l Ph	e Ly:	s Glu	ı Ası	b GT	y Ly:	5 Thi	L Let	ı val	. Ser	Lys>
34	10			350			360	٥			370			380	
	•		•	•		•		•	•		*	•	<b>t</b>	•	
AAA	GT	A AC	T TC	C AA	A GA	C AA	G TC	A TC	A AC	A GA	A GA	A AA	A TT	CAA C	GAA
لمشك	CA	т тс	A AG	GTT	T CT	G TT	C AG	T AG	T TG	T CT	I CI	T TT	AA T	3 TTM	CIT
Lys	Va	1 Th	ır Se	r Ly	s As	p Ly	s Se	r Se	r Th	r Gl	u Gl	u Ly:	s Ph	e Asi	Glu>

FIGURE 29 (1 of 3)

#### B-31 OSP A/ B-31 OSP B FUSION

	390	-		4	00			410			420	)			30.
•	•		•		•	•		•		•	•		•		•
AAA	GGT	GAA	GTA	TCT	GAA	AAA	. ATA	ATA .	ACA	AGA	GCA	GAC	GGA	ACC	AGA
TTT	CCA	CTT	CAT	AGA	CII	TIT	TAT	TAT	TGI	TCI	CGI	, CIG	CCI	TG	TCT
Lys	Gly	Glu	Val	Ser	Glu	. Lys	Ile	Ile	Thr	Arg	Ala	Asp	Gly	The	Arg>
		440			450				60			470	•		
•		•		•	•		•	7	•	٠.		470 •		•	480
CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCĨ	A 2 2	GAG
GAA	CTT	ATG	TGT	CCT	AAT	TIT	TCG	CTA	CCT	AGA	CCT	TTT	CGA	TT	<u> </u>
Leu	Glu	Tyr	Thr	Gly	Ile	Lys	Ser	Asp	Ğly	Ser	Ğly	Lys	Ala	Lys	Glu>
		4:	90			500			510			5	20		
	*		•	•		•		•	•		•		•	•	
GTT	TTA	AAA	GGC	TAT	GTT	CTT	GλA	GGA	ACT	CTA	ACT	GCT	GAA	AAA	ACA
CAA	AAT	TTT	CCG	ATA	CAA	GAA	CII	CCT	TGA	GAT	TGA	CGA	CTT	TIT	TGT
vaı	Leu	rys	GIA	TYT	val	Leu	Glu	Gly	Thr	Leu	Thr	Ala	Glu	Lys	Thr>
530			540			5:	50			560			570		
•		•	•		•		•	•		•		•	•	٠	•
ACA	TTG	GTG	GTT	AAA	GAA	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT.	TCA
TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	TAA	AGT
1111	reu.	Val	Val	Lys	GIU	GIA	Thr	Vai	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
58	30		9	590			600			61	10			20.	
	•	•		•		• .	•		•		•	•		•	
AAA	TCT	GGG	GAA	GTT	TCA	GTT	GAA	CTI	AAT	GAC	ACT	GAC	AGT	AGT	GCT
LVS	Ser	GIV	Glu	Va 1	AGT Ser	UAA Val	CIT	GAA	TTA	CTG	TGA	CTG	TCA	TCA	CGA Ala>
		Oly	014	V 4.1	261	AGI	Giu	reu	ASII	ASP	Inr	ASP	Ser	Ser	Ala>
	630			64	0		$\epsilon$	5'0			660			67	70
CCT	» CT	335.	* * * * * * * * * * * * * * * * * * * *	<b>1</b> CT	•			•		•	•		•		•
CGA	TGA	TATA	that.	TC1	CCT	CCA	100	<b>ጸ</b> ለገ	CTC	AGT TCA	ACT	AGC	ACT	TTA	ACA
λla	Thr	Lys	Lys	Thr	Ala	Ala	Tro	ASD	ASD	Ser	Thr	TCG.	TGA	AAT	TGT Thr>
		_	_						···op		•••	Jei	1111	Leu	1111.>
_	€	80			690			70	0		7	10			720.
ארייני ע	» Cm	~~	C10	•	*		•		•	•		•		•	•
AII AAT	TCA	CCA	CTC	TCG	AAA	AAA	ACT	AAA	GAT	TTG	CTG	TTC	TTA	ACA	GAT
Ile	Ser	Ala	ASD	Ser	LVS	INC	Thr	Tare	ACD	AAC	CAC	AAG .	AAT	TGT	CTA Asp>
					_, _	<b>-</b> 2, 5		Dy S	nsp	Den	Val	Pne	ren	Inr	Asp>
		73	<b>10</b> .		7	40			750			76	0		
	*	·	•	•		•		•	•		•		•	•	
GGT	ACA	ATT	ACA	GTA	CAA	CAA	TAC	AAC	ACA	GCT	GGA	ACC .	AGC	CTA	GAA
GIV	TOI	TIA	The	CAT Val	GIT Gla	GIT Cl-	ATG	TTG	TGT	CGA	CCT	TGG '	TCG	GAT	CTT
			* * 1 T	* C T	GIN	$\sigma_{TU}$	IAL	ASD	Inr	Ala	GIA	Thr	Ser	Leu	Glu>

FIGURE 29 (2 of 3)

B-31 OSP A/ B-31 OSP B FUSION

770 780 790 800 810

GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT TTA

CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA AAT

Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala Leu>

820

AAA TAA TTT ATT Lys \*\*\*>

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

nce Range: 1 to 1401

		:	10			20			30			•	40		
	•		• .	•		•		•	•		•		•	•	
															GCA
															CGT
Met	Lys	Lys	Tyr	Leu	Leu	GIÀ	116	GIY	Leu	lle	Leu	Ala	Leu	Ile	Ala>
50			60			. 7	70			80			90		
•		*	•		•		•	•		*		•	•		•
					AGC										
															CAT
Cys	Lys	Gln	Asn	Val	Ser	Ser	Leu	ASP	Glu	Lys	Asn	Ser	Val	Ser	Val>
10	00		1	110			120			13	30			140	
	•	•		•		•	•		•		•	•		•	
					ATG										
					TAC										
Asp	Leu	Pro	Gly	Glu	Met	Lys	Val	Leu	Val	Ser.	Lys	Glu	Lys	Asn	Lys>
	150			16	50		•	170			180			19	9.0
•	•	*	•	-	•	•		•		•			•		•
GAC	GGC	AAG	TAC	GAT	CTA	TTA	GCA.	ACA	GTA	GAC	AAG	CTT	GAG	CTT	AAA
CTG	CCG	TTC	ATG	CTA	GAT	TAA	CGT	TGT	CAT	CTG	TTC	GAA	CTC	GAA	TIT
Asp	Gly	Lys	Tyr	Asp	Leu	Ile	Ala	Thr	Val	Asp	Lys	Leu	Glu	Leu	Lys>
	2	200		•	210			22	20		2	230			240
. •	2	200		•	210	-	•	22	20	•	2	230		•	240
	ACT	* TCT			• AAC			TCT	• GGA		CTT	• GAA			* AAA
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG	CAT	AAA TTT
CCT	ACT TGA	TCT AGA	CTA	TTT	AAC TTG	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG	CAT	* AAA
CCT	ACT TGA	TCT AGA Ser	CTA	TTT	AAC TTG Asn	TTA	CCT	TCT AGA	• GGA	CAT	CTT GAA	GAA CTT	CCG Gly	CAT	aaa TTT
CCT	ACT TGA Thr	TCT AGA Ser	CTA Asp 50	TTT Lys	AAC TTG Asn	TTA Asn 260	CCT	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu	GAA CTT Glu 28	CCG Gly 80	CAT Val	AAA TTT Lys>
GCT GCT	ACT TGA Thr	TCT AGA Ser 25	CTA Asp 60 • AGT	TTT Lys	AAC TTG ASD	TTA Asn 260	CCT Gly TTA	TCT AGA Ser	GGA CCT Gly 270	CAT Val	CTT GAA Leu GAC	GAA CTT Glu 28	CCG Gly 80 • CTA	CAT Val	AAA TTT Lys>
GCT GCT GCT CGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA Asp 50 * AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 60 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys> CAA GTT
GCT GCT GCT CGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA Asp 50 * AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 60 AAA TTT	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys>
GCT GCT GCT CGA	ACT TGA Thr GAC CTG	TCT AGA Ser 25	CTA Asp 50 * AGT TCA	TTT Lys AAA TTT	AAC TTG ASD GTA CAT	TTA ASD 260 AAA TTT Lys	CCT Gly TTA AAT	TCT AGA Ser ACA TGT	GGA CCT Gly 270 ATT TAA Ile	CAT Val TCT AGA	CTT GAA Leu GAC CTG	GAA CTT Glu 28 GAT CTA	CCG Gly 80 • CTA GAT	CAT Val GGT CCA	AAA TTT Lys> CAA GTT
GCT CGA Ala	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA Asp 50 * AGT TCA Ser 300	TTT Lys AAA TTT Lys	AAC TTG Asn GTA CAT Val	AAA TTT Lys	CCT Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 28 GAT CTA Asp	CCG Gly 30 CTA GAT Leu	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTT Gln>
GCT CGA Ala	ACT TGA Thr GAC CTG Asp	TCT AGA Ser 25 AAA TTT Lys	CTA Asp 50 * AGT TCA Ser 300	TTT Lys AAA TTT Lys	AAC TTG ASD GTA CAT	AAA TTT Lys	CCT Gly TTA AAT Leu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile	TCT AGA Ser	CTT GAA Leu GAC CTG Asp	GAA CTT Glu 28 GAT CTA Asp	CCG Gly 30 CTA GAT Leu	CAT Val GGT CCA Gly	AAA TTT Lys> CAA GTT Gln>
GCT GGA Ala 290 * ACC TGG	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 25 AAA TTT Lys CTT GAA	CTA ASP  O AGT TCA Ser  300 GAA CTT	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 30 CTA GAT Leu 330 GTA CAT	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GCT GGA Ala 290 * ACC TGG	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 25 AAA TTT Lys CTT GAA	CTA ASP  O AGT TCA Ser  300 GAA CTT	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 30 CTA GAT Leu 330 GTA CAT	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln>
GCT GGA Ala 290 ACC TGG Thr	ACT TGA Thr GAC CTG ASP	TCT AGA Ser 25 AAA TTT Lys CTT GAA	AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys GTT CAA	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG ASP	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 0 * CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT	AAA TTT Lys> CAA GTT Gln> AAA TTT
GCT GGA Ala 290 ACC TGG Thr	ACT TGA Thr GAC CTG Asp ACA TGT	TCT AGA Ser 25 AAA TTT Lys CTT GAA	AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys GTT CAA Val	AAC TTG Asn GTA CAT Val	AAA TTT  AAA TTT  AAA TTT	CCT Gly TTA AAT Leu 10 GAA CTT Glu	TCT AGA Ser ACA TGT Thr	GGA CCT Gly 270 ATT TAA Ile GGC CCG	TCT AGA Ser 320 AAA TTT Lys	CTT GAA Leu GAC CTG Asp ACA TGT	GAA CTT Glu 28 GAT CTA ASD	CCG Gly 0 * CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT
GCT GAAAAAAAAAA	ACT TGA Thr GAC CTG ASP ACA TGT Thr	TCT AGA Ser 25 AAA TTT Lys CTT GAA Leu ACT	CTA ASP  O AGT TCA Ser  300 CTT Glu  TCC	TTT Lys  AAA TTT Lys  GTT CAA Val  350  AAA	AAC TTG Asn GTA CAT Val TTC AAG Phe	TTA ASD 260 AAA TTT Lys AAA TTT Lys AAA AAA TTT Lys	CCT Gly TTA AAT Leu 10 GAA CTT Glu 360	TCT AGA Ser ACA TGT Thr GAT CTA Asp	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser 20 AAA TTT Lys 31	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 28 GAT CTA Asp CTA GAT Leu	CCG Gly 30 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>
GCT GGA Ala 290 * ACC TGG Thr	ACT TGA Thr GAC CTG ASP ACA TGT Thr	TCT AGA Ser 25 AAA TTT Lys CTT GAA Leu ACT TGA	AGT TCA Ser 300 GAA CTT Glu	TTT Lys AAA TTT Lys GTT CAA Val 350	AAC TTG ASN GTA CAT Val TTC AAG Phe	AAA TTT Lys AAA TTT Lys AAA TTT Lys	CCT Gly TTA AAT Leu 10 GAA CTT Glu 360 TCA AGT	TCT AGA Ser ACA TGT Thr CTA ASP	GGA CCT Gly 270 ATT TAA Ile GGC CCG Gly	TCT AGA Ser AAA TTT Lys GAA CTT	CTT GAA Leu GAC CTG ASP ACA TGT Thr	GAA CTT Glu 28 GAT CTA ASP CTA GAT Leu	CCG Gly 0 CTA GAT Leu 330 GTA CAT Val	CAT Val GGT CCA Gly TCA AGT Ser 80 AAT TTA	AAA TTT Lys> CAA GTT Gln> AAA TTT Lys>

FIGURE 30 (1 of 4)

## B-31 OAP A/ B-31 OSP B / B-31 OSPC FUSION

390		400		4:	10			420			43	Ó
•	•	•	•		•	•	•	•	,	•		•
AAA GGT GAA	GTA TC	T GAA	AAA	ATA A	ATA	ACA	AGA	GCA	GAC	GGA	ACC	AGA
TTT CCA CTT	CAT AG	A CTT	TTT	TAT :	TAT	TGT	TCT	CGT	CTG	CCT	TGG	TCI
Lys Gly Glu	Val Se	er Glu	Lys	Ile	Ile	Thr	Arg	ALZ	ASP	GIĀ	Thr	Arg>
440		450			46	n		۵	70			480
440		430		•	40	•	•		*		•	*
CTT GAA TAC	ACA GO	TTA A	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA	GAG
GAA CTT ATG	TGT CC	TAA T	TTT	TCG	CTA	CĊT	AGA	TOOT	TTT	CGA	TTT	CIC
Leu Glu Tyr	Thr Gl	ly Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys	Glu>
49	90	5	500		_	510		_	52	20		
•	•		~~~	C	CCY	y C.J.	CT 3	እርጥ	CCT	CAA	222	
GTT TTA AAA CAA AAT TTT	GGC TA	AT GIT	CIT	CTT	CCT	TGL	CIA	AC7	CCF	CAA	July Serve	ACA.
Val Leu Lys	CCG A	IM CAM	Leu	Glu	GIV	Thr	Leu	Thr	Ala	Glu	Lvs	Thr>
val red rys	GIA 17	yı var	בים	020							-2-	
530	540		55	50		9	560			570		
• •	•	•		•	•		•		•	•		. •
ACA TTG GTG	GTT A	aa gaa	GGA	ACT	GTT	ACT	TTA	AGC	AAA	AAT	ATT	TCA
TGT AAC CAC	CAA T	TT CTT	CCT	TGA	CAA	TGA	TAA	TCG	TIT	TTA	TAA	AGT
Thr Leu Val	Val L	ys Glu	Gly	Thr	Val	Thr	Leu	Ser	Lys	Asn	Ile	Ser>
500	50	0		600			6:	10			520	
580	59	0 *	•	600		•	6:	10	•		520	
AAA TCT GGG	GAA G	TT TCA	GTT	• GAA	CTT	* - AAT	GAC	ACT	• GAC	AGT	AGT	GCT
AAA TCT GGG	GAA G	TT TCA	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TCT GGG	GAA G	TT TCA	CAA	GAA CTT	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA
AAA TCT GGG TTT AGA CCC Lys Ser Gly	GAA G	TT TCA AA AGT al Ser	CAA	GAA CTT Glu	GAA Leu	TTA	GAC CTG	ACT TGA Thr	CTG	AGT TCA	AGT TCA Ser	CGA Ala>
AAA TCT GGG	GAA G	TT TCA	CAA	GAA CTT Glu	GAA	TTA	GAC CTG	ACT TGA	CTG	AGT TCA	AGT TCA	CGA Ala>
AAA TCT GGG TTT AGA CCC Lys Ser Gly 630	GAA G CTT C Glu V	TT TCA AA AGT al Ser	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn	GAC CTG Asp	ACT TGA Thr	CTG Asp	AGT TCA Ser	AGT TCA Ser	CGA Ala>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA	GAA G CTT C Glu V	TT TCA AA AGT al Ser 640	CAA Val	GAA CTT Glu	GAA Leu 650	TTA Asn GAC	GAC CTG Asp	ACT TGA Thr 660	ASP AGC	AGT TCA Ser	AGT TCA Ser 6	CGA Ala> 70 ACA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT	GAA G CTT C Glu V	TT TCA AA AGT al Ser 640 CT GCA	CAA Val • • • GCT	GAA CTT Glu TGG	GAA Leu 650 AAT TTA	TTA Asn GAC CTG	GAC CTG Asp AST TCA	ACT TGA Thr 660 ACT	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA	GAA G CTT C Glu V	TT TCA AA AGT al Ser 640 . CT GCA GA CGT Thr Ala	CAA Val GCT CGA Ala	GAA CTT Glu TGG	GAA Leu 550 AAT TTA Asn	TTA Asn GAC CTG Asp	GAC CTG Asp AST TCA	ACT TGA Thr 660 ACT	AGC TCG Ser	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT Thr>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT	GAA G CTT C Glu V	TT TCA AA AGT al Ser 640 CT GCA	CAA Val GCT CGA Ala	GAA CTT Glu TGG	GAA Leu 550 AAT TTA Asn	TTA Asn GAC CTG	GAC CTG Asp AST TCA	ACT TGA Thr 660 ACT	ASP AGC TCG	AGT TCA Ser ACT TGA	AGT TCA Ser 6 TTA AAT	CGA Ala> 70 ACA TGT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Chr Ala	CAA Val GCT CGA	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Thr Ala 690	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA ASD	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Thr Ala 690 AGC AAF	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Thr Ala 690 AGC AAF	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630 GCT ACT AAA CGA TGA TTT Ala Thr Lys  680 ATT AGT GCT TAA TCA CGA	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Thr Ala 690 AGC AAF	CAA Val GCT CGA Ala	GAA CTT Glu TGG ACC Trp	GAA Leu 650 AAT TTA Asn 7	GAC CTG Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser 710 TTCC AAGC	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G CTT C Glu V AAA A TTT T Lys T	TT TCA AA AGT al Ser 640 CT GCA GA CGT Chr Ala 690 AGC AAF	CAA Val GCT CGA Ala AAAA TTTT Lys 740	GAA CTT Glu TGG ACC Trp ACT TGA	GAA Leu 550 AAT TTA ASD 7 AAA TTT Lys	GAC CTG Asp 00 GAT CTA Asp	GAC CTG Asp AGT TCA Ser	ACT TGA Thr 660 ACT TGA Thr	AGC TCG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu ACA TGT	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA Asp>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G CTT C Glu V AAA A TTT T Lys T CGAC A CTG T A Asp S	TT TCA AA AGT al Ser 640 ACT GCA Chr Ala 690 AGC AAF	CAA Val GCT CGA Ala AAA TTTT Lys 740	GAA CTT Glu TGG ACC Trp ACT TGA Thr	GAA Leu 550 AAT TTA ASD 7 AAA TTT Lys	GAC CTG Asp 00 CTI CTI Asr 750	GAC CTG Asp AGT TCA Ser TTG AAC	ACT TGA Thr 660 ACT TGA Thr CGA Thr	AGC TCG Ser 710 TTC AAG	AGT TCA Ser ACT TGA Thr	AGT TCA Ser 6 TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA ASP>
AAA TCT GGG TTT AGA CCC Lys Ser Gly  630  GCT ACT AAA CGA TGA TTT Ala Thr Lys  680  ATT AGT GCT TAA TCA CGA Ile Ser Ala	GAA G CTT C Glu V AAA A TTT T Lys T CGAC A CTG T A Asp S	TT TCA AA AGT al Ser 640 ACT GCA CAT Ala AGC AAA TCG TTT Ser Lys	CAA Val GCT CGA Ala TTTT Lys 740 A CAU	GAA CTT Glu TGG ACC Trp ACT TGA TAC	GAA Leu 550 AAT TTA Asn 7 AAA TTI Lys AAC TTO	GAC CTG ASP 00 CTA CTA ASE 750 CACA CTA	GAC CTG ASP AGT TCA Ser AAC Lev	ACT TGA Thr 660 ACT TGA Thr CGGGGA CCG	AGC TCG Ser 710 Phe	AGT TCA Ser ACT TGA Thr TAAT Leu 60	AGT TCA Ser 6 TTA AAT Leu ACA TGT Thr	CGA Ala> 70 ACA TGT Thr> 720 GAT CTA ASP> A GAA CTT

FIGURE 30 (2 of 4)

#### B-31 OSP A/ B-31 OSP B / B-31 OSP C FUSION

770			780	ļ.		7	90			800			81	`	
•		•	•		•		•	•		•		•		,	
GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTI	TCA	GAG	CTI	· AAA	AA C	GCI	TTA
CCI	` AGT	CGI	, TCY	CTI	TAA	TTT	TTA	GAA	AGT	CIC	GAA	TT	TTO	: רה:	227
Gly	Ser	Ala	Ser	Glu	Ile	Lys	Asn	Leu	Ser	Glu	Leu	Lys	ÀS:	: Ala	Leu>
8	20			830			840			8	50			550	
	•			•		• .	•		•			•		•	
AAA	ATG	GCT	TAA	AAT	TCA	GGG	AAA	GAT	GGG	AAT	ACA	TCT	GCA	TAA .	ICI
111	MAC	LUA	TTA	TTA	AGT	600	TTT	CTA	CCC	TTA	TGT	AGA	CGI	TTA	AGA
Lys	nec	VIG	ASII	ASII	Sei	GIY	Lys	Asp	GTA	ASD	-Thr	Ser	Ala	Asn	Ser>
	870			8	80		1	890 <sup>°</sup>			900			9	10
•	•		•		•	•		•		•	•		•		
GCT	GAT	GAG	TCT	GTT	AAA	GGG	CCT	AAT	CTT	ACA	GAA	ATA	AGT	AAA	ልልል
CGA	CTA	CIC	AGA	CAA	TTT	CCC	GGA	TTA	GAA	TGT	CTT	TAT	TCA	TIT	LIL
AIG	ASP	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Lys	_7,2>
	. 9	920			930			9.	40		9	950			960
•		•		•	*		•		•	•		•		•	•
ATT	ACG	GAT	TCT	TAA	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG
TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAS	نبلب	CGC
TITE	Thr	Asp	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
₫¹.		۰.	70			980			000						
	•	,	*	•		*		•	990		. • •	100	00	_	
TTG	CTG	TCA	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	CCT	AAA	
⊕ AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAL	CCZ	شلك	سنت
∘∉Leu	_														
	Leu	Ser	Ser	Ile	Asp	Glu	Ile	Ala	Ala	Lys	Ala	Ile	Gly	Lys	Lys>
010	Leu	Ser	Ser 1020	Ile	Asp	Glu 103	Ile	Ala	Ala	Lys 40	Ala	Ile	Gly	Lys	Lys>
010		Ser	Ser 1020	Ile	Asp	Glu 103	Ile O	Ala •	Ala 10	Lys 40	Ala	Ile	Gly 050	Lys	•
010 • ATA	CAC	Ser CAA	Ser 1020 •	Ile AAT	Asp • GGT	Glu 103 TTG	Ile 0 • GAT	Ala * ACC	Ala 10 GAA	Lys 40 *	Ala	Ile 1	050 *	Lys	• TC
O10 ATA TAT	CAC GTG	· CAA	Ser 1020 AAT TTA	Ile AAT TTA	Asp GGT CCA	Glu 103 TTG AAC	O GAT CTA	Ala * ACC TGG	Ala 10 GAA CTT	Lys 40 TAT ATA	Ala AAT TTA	Ile  CAC GTG	Gly 050 AAT TTA	Lys GGA	TCA
O10 ATA TAT	CAC GTG	· CAA	Ser 1020 AAT TTA	Ile AAT TTA	Asp GGT CCA	Glu 103 TTG AAC	O GAT CTA	Ala * ACC TGG	Ala 10 GAA CTT	Lys 40 TAT ATA	Ala AAT TTA	Ile  CAC GTG	Gly 050 AAT TTA	Lys GGA	• TC
O10 ATA TAT	CAC GTG His	· CAA	Ser LO20 AAT TTA Asn	Ile AAT TTA	Asp GGT CCA	Glu 103 TTG AAC Leu	O GAT CTA	Ala * ACC TGG	Ala 10 GAA CTT	Lys 40 TAT ATA	Ala AAT TTA Asn	Ile  CAC GTG	Gly 050 AAT TTA Asn	Lys GGA	TCA
ATA TAT Ile	CAC GTG His	CAA GTT Gln	Ser 1020 AAT TTA Asn	AAT TTA Asn	GGT CCA Gly	Glu 103 TTG AAC Leu	O TA ASP	ACC TGG Thr	GAA CTT Glu	Lys 40 TAT ATA Tyr 109	Ala AAT TTA Asn 0	Ile L CAC GTG His	Gly 050 AAT TTA Asn	Lys GGA CCT Gly 00	TCA AGT Ser>
ATA TAT Ile 106	CAC GTG His	CAA GTT Gln	Ser 1020 AAT TTA Asn 10 GGA	AAT TTA Asn	Asp GGT CCA Gly	TTG AAC Leu	O TA ASP O80	Ala ACC TGG Thr	GAA CTT Glu	Lys  140  TAT  ATA  Tyr  109	Ala AAT TTA Asn 0	Ile  CAC GTG His	Gly 050 AAT TTA Asn	Lys GGA CCT Gly 00	TCA AGT Ser>
ATA TAT Lile 106 TTG AAC	CAC GTG His_ TTA AAT	CAA GTT Gln GCG CGC	AAT TTA Asn 10 GGA CCT	AAT TTA Asn CGT GCA	GGT CCA Gly TAT	TTG AAC Leu  GCA CGT	GAT CTA ASP 080	Ala ACC TGG Thr TCA AGT	GAA CTT Glu ACC TGG	Lys  140  TAT  ATA  Tyr  109  CTA  GAT	Ala AAT TTA ASD 0 ATA	Ile  CAC GTG His	Gly 050 AAT TTA Asn 11 CAA	GGA CCT Gly	TCA AGT Ser>
ATA TAT Ile 106 TTG AAC Leu	CAC GTG His 50 • TTA AAT Leu	CAA GTT Gln GCG CGC	AAT TTA Asn 10 GGA CCT	AAT TTA Asn 070 CGT GCA Arg	GGT CCA Gly TAT ATA Tyr	TTG AAC Leu  GCA CGT	GAT CTA ASP 080 ATA TAT	ACC TGG Thr TCA AGT Ser	GAA CTT Glu ACC TGG	Lys  140  TAT  ATA  Tyr  109  CTA  GAT	Ala AAT TTA ASD 0 ATA	Ile  CAC GTG His	Gly 050 AAT TTA Asn 11 CAA	GGA CCT Gly	TCA AGT Ser>
ATA TAT Ile 106 TTG AAC Leu	CAC GTG His_ TTA AAT	CAA GTT Gln GCG CGC	AAT TTA Asn 10 GGA CCT	AAT TTA Asn CGT GCA	GGT CCA Gly TAT ATA Tyr	TTG AAC Leu  GCA CGT	GAT CTA ASP 080 ATA TAT	Ala ACC TGG Thr TCA AGT	GAA CTT Glu ACC TGG	TAT ATA Tyr 109 CTA GAT Leu	Ala AAT TTA ASD 0 ATA	Ile  CAC GTG His	Gly 050 AAT TTA Asn 11 CAA	GGA CCT Gly	TCA AGT Ser> TTA AAT Leu>
ATA TAT Ile 106 TTG AAC Leu	CAC GTG His TTA AAT Leu	CAA GTT Gln GCG CGC Ala	AAT TTA Asn 10 GGA CCT Gly	AAT TTA Asn 70 CGT GCA Arg	GGT CCA Gly TAT ATA Tyr	TTG AAC Leu GCA CGT Ala	GAT CTA ASP 080 ATA TAT Ile	ACC TGG Thr TCA AGT Ser	GAA CTT Glu • ACC TGG Thr	Lys  40  TAT  ATA  Tyr  109  CTA  GAT  Leu  1	Ala AAT TTA Asn 0 ATA TAT Ile 140	Ile  CAC GTG His  AAA TTT Lys	OSO AAT TTA ASD II CAA GTT GID	GGA CCT Gly 00 AAA TTT Lys	TCA AGT Ser> TTA AAT Leu> 0
ATA TAT Ile 106 TTG AAC Leu 1	CAC GTG His TTA AAT Leu	CAA GTT Gln GCG CGC Ala	AAT TTA ASD 10 GGA CCT Gly AAA	AAT TTA ASD OTO CGT GCA Arg	GGT CCA Gly TAT ATA Tyr	Glu 103 TTG AAC Leu 1 GCA CGT Ala	Ile  O GAT CTA ASP  OBO ATA TAT Ile  II	ACC TGG Thr TCA AGT Ser	GAA CTT Glu ACC TGG Thr	Lys  40  TAT  ATA  Tyr  109  CTA  GAT  Leu  1	Ala AAT TTA Asn 0 ATA TAT Ile 140 ATT	Ile  CAC GTG His  AAA TTT Lys	Gly  050  AAT  TTA  Asn  II  CAA  GTT  GIn	GGA CCT Gly 00 AAA TTT Lys	TCA AGT Ser> TTA AAT Leu> 0
ATA TAT Ile 106 TTG AAC Leu 1 GAT CTA	CAC GTG His TTA AAT Leu	CAA GTT Gln GCG CGC Ala	AAT TTA ASD GGA CCT Gly AAA TTT	AAT TTA ASD CGT GCA Arg 112 AAT TTA	GGT CCA Gly TAT ATA Tyr GAA CTT	Glu 103 TTG AAC Leu 1 GCA CGT Ala GGA CCT	GAT CTA ASP 080 ATA TAT Ile 11 TTA AAT	ACC TGG Thr TCA AGT Ser 30	GAA CTT Glu ACC TGG Thr	Lys 40 TAT ATA Tyr 109 CTA GAT Leu 1 AAA TTT	Ala AAT TTA Asn 0 ATA TAT Ile 140 ATT	CAC GTG His	Gly  O50  AAT  TTA  ASN  II  CAA  GTT  GIN	GGA CCT Gly 00 AAA TTT Lys	TCA AGT Ser> TTA AAT Leu> 0

FIGURE 30 (3 of 4)

## B-31 OSP A / B-31 OSP B/ B-31 OSP C FUSION

	1160 1170							118	80		11	.90		נ	200
•		•		•	•		•		*	*		•		•	•
AAA	TGT	TCT	GAA	ACA	TTT	ACT	TAA	AAA	TTA	AAA	GCA	AAA	CAC	ACA	GAT
TTT	ACA	AGA	CII	TGT	AAA	TGA	TTA	TTT	AAT	1.1.1	CGI	111	616	161	CIA
Lys	Cys	Ser	Glu	Thr	Phe	Thr	Asn	Lys	Leu	Lys	Ala	Lys	Ris	Thr	Asp>
		12:	10		12	20		1	1230			124	0		
	•		•	•		•		•	•		•		•	*	
CTT	GGT	AAA	GAA	GGT	GTT	ACT	GAT	GCT	GAT	GCA	AAA	GAA	GCC	TTA	TTA
GAA	CCA	TIT	CTT	CCA	CAA	TGA	CTA	CGA	CTA	CGT	TIT	CTT	CGG	TAA	AAT
Leu	Gly	Lys	Glu	Gly	Val	Thr	Asp	Ala	Asp	Ala-	Lys	Glu	Ala	Ile	Leu>
			1260			12	70		1	280			1290		
1250			1760		_	44				. •		*	′ <b>•</b>		•
*		•	•						~~	C	C2.2	حصت	CCA	222	ተጥ አ
AAA	ACA	TAA	GGT	ACT	AAA	ACT	AAA	GGT	661	GAA	OAA	CII	CCT	STATE OF THE PERSON SERVICES	222
TTT	TGT	TTA	CCA	TGA	TTT	TGA	TTT	CCA	CGA	Cil	CII	GAA	~3	111	WW.1
Lys	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	GIA	GIU	Leu	GIÀ	Lys	Leu>
12	00		1	310			1320			13	30		1	340	
1.5	•	•		•		•	•		•		•	•		•	•
TTT	GAA	TCA	GTA	GAĞ	GTC	TTG	TCA	AAA	GCA	GCT	አልል	GAG	ATG	CTT	GCT
222	СТТ	· ACT	רבר י	CTC	CAG	AAC	AGT	, TTT	CGI	, CGY	TTT	CTC	TAC	GAA	CGA
Phe	Glu	Ser	. Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
	<b>-</b> -				<b>C</b> D		1	370			1380			13	90
	1350	)		13	00	_		.5,0			*		•		•
•	•	•							, Cubu	, CTC	GC:	CAA	YCT.	CCF	AAA
AAT	TC	A GT	AAA 1	GAG	CIT	ACA	AGG		011	010			TO 1	CC7	AAA
TTA	A AG	נ כאז	, TTI	CIC	GAA	TG1	TCC	GGA	CAA	CAC		CII	104	. GG1	TTT
Asr	Sei	· Va	l Lys	Glu	Leu	Thi	Sei	Pro	Va:	. Val	. Ala	GIU	ser	PIO	Lys>

1400

AAA CCT TAA TTT GGA ATT Lys Pro \*\*\*>

FIGURE 30 (4 of 4)

## B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

				10			20			30	)			40		
		•		•	•	•	•	-	٠.,	•	•	•		•	•	•
	ATG	AAA	AAG	AAT	, YCY	ATT A	AGT	, ecc	ATA	TTA	ATC	AC1	TT	TIT	TT	A TTT
	TAC	TTI	TTC	TTA	TGI	AAT	TCA	CGC	TAT	' AAT	' TAC	TGA	L AA7	LAA 1	EAA I	AAA
	met	Lys	·	AST	ını	Leu	Ser	. YIS	Ile	Leu	Met	Thr	Leu	Phe	Let	Phe>
	50			60				70			80			90	,	
	•		•	•		•		•	•		•		•	•		•
	ATA	TCT	TGT	' AAT	TAA	TCA	GGG	AAA	GAT	GGG	AAT	' ACA	TCI	, GCA	AAT	TCT
	TAT	AGA	ACA	TTA	TTA	AGT	CCC	TTT	CTA	CGC	TTA	-TGT	AGA	CGT	מדים	863
	Ile	Ser	Cys	Asn	Asn	Ser	Gly	Lys	Asp	Gly	Asn	Thr	Ser	Ala	Asn	Ser>
	1	00			110			120			. 1	30			140	
		•	•		•		•	•		•	-	•	•		T # 0	
	GCT	GAT	GAG	TCT	GTT	AAA	GGG	CCT	AAT	CTT	ACA	GAA	ATA	AGT	AAA	444
	CGA	CTA	CTC	AGA	CAA	TTT	CCC	GGA	TTA	GAA	TGT	CTT	TAT	TCA	لملث	سنت
	Ala	Asp	Glu	Ser	Val	Lys	Gly	Pro	Asn	Leu	Thr	Glu	Ile	Ser	Lys	Lys>
		150			1	60			170			100				
	• .			•	_	•	•		+		•	180			1:	90
	ATT	ACG	GAT	TCT	AAT	GCG	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	ece.
•r -	TAA	TGC	CTA	AGA	TTA	CGC	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	حيت	CGC
	Ile	Thr	Asp	Ser	Asn	Ala	Val	Leu	Leu	Ala	Val	Lys	Glu	Val	Glu	Ala>
		,	200			210				20						
,	•		•		•			•	44	*	•		230		•	245
	TTG	CTG	TCA	TCT	ATA	GAT	GAA	ATT	GCT	GCT	AAA	GCT	ATT	CCT	222	222
	AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAA	CCA	طحلمك	444
	Leu	Leu	Ser	Ser	Ile	Asp	Glu	Ile	Ala	Ala	Lys	Ala	Ile	Gly	Lys	Lys>
			2 5	50		-	260			270			2.0			
		•		*	•	•	•	,	•	210		•	28	3 U		
	ATA	CAC	CAA	AAT	AAT	GGT	TTG	GAT	ACC	GAA	TAT	AAT	CAC	AAT	GG2	TCA
	TAT	GTG	GTT	TTA	ATT	CCA	AAC	CTA	TGG	CTT	ATA	TTA	GTG	TTL	CCT	ACT.
	Ile	His	Gln	Asn	Asn	Gly	Leu	Asp	Thr	Glu	Tyr	Asn	His	Asn	Gly	Ser>
2	90			300			31	LO		3	20			220		
	•		•	•		•		•	•		•		•	330		•
	TTG	TTA	GCG	GGA	CGT	TAT	GCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA
	AAC	AAT	CGC	CCT	GCA	ATA	CGT	TAT	AGT	TGG	GAT	TAT	TTT	GTT	TTT	TAA
	Leu	Leu	Ala	Gly	Arg	Tyr	Ala	Ile	Ser	Thr	Leu	Ile	Lys	Gln	Lys	Leu>
	34	0		3	50			360			37	'n		2	80	
		•	•		•		*	•		•		•	•			
	GAT	GGA	TTG	AAA	TAA	GAA	GGA	TTA	AAG	GAA	AAA	ATT	GAT	GCG	GCT	AAG
	CTA	CCT	AAC	TTT	TTA	CTT	CCT	TAA	TTC	CTT	TTT	TAA	CTA	CGC	CGN	<u> ጥ</u> ጥር
	Asp	Gly	Leu	Lys	Asn	Glu	Gly	Leu	Lys	Glu	Lys	Ile	Asp	Ala	Ala	Lys>

#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

_	390			4 (	00		4	110			420			4:	30
מממ	TCT.	عرب	440	ACA	TTT	γ (⊸1. -	TAA	444	<b>4TT</b>	227	GCA	222	ראַר	AC2	CAT
					AAA										
															Asp>
-	•							_				_			
•	4	140		•	450		•	4 (	50		4	170	•	•	480
CTT	GGT	AAA	GAA	GGT	GTT	ÄCT	GAT	GCT	GAT	GCA	AAA	GAA	GCC	ATT	TTA
					CAA										
Leu	Gly	Lys	Glu	Gly	Val	Thr	Asp	Ala	Asp	Āla	Lys	Glu	Ala	Ile	Leu>
		49	a n			500			510			5.5	20		
	•	•••	•	•	•	•	•	•	•		•		•	•	
AAA	ACA	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	CTT	GGA	AAA	TTA
					TTT										
Ĺys	Thr	Asn	Gly	Thr	Lys	Thr	Lys	Gly	Ala	Glu	Glu	Leu	Gly	Lys	Leu>
530			540			S	50			560			570		
•		• 1	•		•		•	. •		•		•	•		•
TTT	GAA	TCA	GTĄ	GAG	GTC	TTG	TCA	AAA	GCA	GCT	AAA	GAG	ATG	CTT	GCT
					CAG										
Phe	Glu	Ser	Val	Glu	Val	Leu	Ser	Lys	Ala	Ala	Lys	Glu	Met	Leu	Ala>
5.0	30		,	590			600			63	LO		4	20	
٠, ر	•	•	•	•	,	•			*		•	•	Ì	*	
AAT	TCA		AAA	• GAG	CTT		AGC			GTG	GCA		AGT	CCA	
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC	GAA	TGT	AGC TCG	GGA	CAA	GTG CAC	.* GCA CGT	CTT	AGT TCA	CCA GGT	TTT
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC		TGT	AGC TCG	GGA	CAA	GTG CAC	.* GCA CGT	CTT	AGT TCA	CCA GGT	TTT
AAT TTA	TCA AGT	CAA	AAA TTT	GAG CTC Glu	GAA	TGT	AGC TCG Ser	GGA	CAA	GTG CAC	.* GCA CGT	CTT	AGT TCA	CCA GGT	TTT Lys>
AAT TTA	TCA AGT Ser	CAA	AAA TTT	GAG CTC Glu	GAA Leu	TGT	AGC TCG Ser	GGA Pro	CAA	GTG CAC	GCA CGT Ala	CTT	AGT TCA	CCA GGT Pro	TTT Lys>
AAT TTA Asn	TCA AGT Ser 630 CCT	CAA Val	AAA TTT Lys CAA	GAG CTC Glu 64	GAA Leu 40 • GTT	TGT Thr AGC	AGC TCG Ser	GGA Pro 550 *	CAA Val GAC	GTG CAC Val	GCA CGT Ala 660	CTT Glu AAC	AGT TCA Ser	CCA GGT Pro 67	TTT Lys>
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA	CAA Val AAG TTC	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 40 • GTT CAA	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 50 * CTT GAA	CAA Val GAC CTG	GTG CAC Val	GCA CGT Ala 660 AAA TTT	CTT Glu AAC TTG	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys> 0 TCA AGT
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA	CAA Val AAG TTC	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 40 • GTT CAA	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 50 * CTT GAA	CAA Val GAC CTG	GTG CAC Val	GCA CGT Ala 660 AAA TTT	CTT Glu AAC TTG	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys>
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 40 • GTT CAA	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 550 * CTT GAA Leu	CAA Val GAC CTG	GTG CAC Val	GCA CGT Ala 660 AAA TTT Lys	CTT Glu AAC TTG	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys> 0 TCA AGT
AAT TTA Asn • AAA TTT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys	AAA TTT Lys CAA GTT	GAG CTC Glu 64 AAT TTA	GAA Leu 10 GTT CAA Val	TGT Thr AGC TCG	AGC TCG Ser AGC TCG	GGA Pro 550 * CTT GAA Leu	CAA Val GAC CTG Asp	GTG CAC Val	GCA CGT Ala 660 AAA TTT Lys	CTT Glu AAC TTG Asn	AGT TCA Ser * AGC TCG	CCA GGT Pro 67 GTT CAA	TTT Lys>  C TCA AGT Ser>
AAT TTA ASN AAA TTT Lys	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680	AAA TTT Lys CAA GTT Gln	GAG CTC Glu 64 AAT TTA Asn	GAA Leu 10 GTT CAA Val 690	TGT Thr AGC TCG Ser	AGC TCG Ser AGC TCG Ser	GGA Pro 550 * CTT GAA Leu 70	CAA Val GAC CTG Asp	GTG CAC Val GAG CTC Glu	GCA CGT Ala 660 AAA TTT Lys	AAC TTG Asn	AGT TCA Ser * AGC TCG Ser	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 * TCA AGT Ser> 720 AAC
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680 TTG AAC	AAA TTT Lys CAA GTT Gln CCT GGA	GAG CTC Glu 64 AAT TTA ASD	GAA Leu 10 GTT CAA Val 690 GAA CTT	TGT Thr AGC TCG Ser ATG TAC	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 550 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG ASD 110	AGT TCA Ser AGC TCG Ser GAA CTT	CCA GGT Pro 67 GTT CAA Val	TTT Lys> 0 * TCA AGT Ser> 720 AAC
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	CAA Val AAG TTC Lys 680 TTG AAC	AAA TTT Lys CAA GTT Gln CCT GGA	GAG CTC Glu 64 AAT TTA ASD	GAA Leu 10 GTT CAA Val 690 GAA CTT	TGT Thr AGC TCG Ser ATG TAC	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 550 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG ASD 110	AGT TCA Ser AGC TCG Ser GAA CTT	CCA GGT Pro 67 GTT CAA Val	TIT Lys> 0 * TCA AGT Ser> 720 AAC
AAT TTA ASD AAA TTT Lys GTA CAT	TCA AGT Ser 630 CCT GGA Pro	AAG TTC Lys 680 TTG AAC Leu	AAA TTT Lys CAA GTT Gln CCT GGA	GAG CTC Glu 64 AAT TTA ASD	GAA Leu 10 GTT CAA Val 690 GAA CTT Glu	TGT Thr AGC TCG Ser ATG TAC	AGC TCG Ser AGC TCG Ser AAA TTT	GGA Pro 550 * CTT GAA Leu 70 GTT CAA	GAC CTG Asp	GTG CAC Val GAG CTC Glu GTA CAT	GCA CGT Ala 660 AAA TTT Lys AGC TCG	AAC TTG Asn 710 * AAA TTT Lys	AGT TCA Ser AGC TCG Ser GAA CTT	CCA GGT Pro 67 GTT CAA Val	TTT Lys> 0 * TCA AGT Ser> 720 AAC
AAT TTA ASD AAA TTT Lys GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro	AAG TTC Lys 680 TTG AAC Leu	AAA TTT Lys CAA GTT Gln CCT GGA Pro	GAG CTC Glu 64 AAT TTA Asn GGT CCA Gly	GAA Leu 10 GTT CAA Val 690 GAA CTT Glu	TGT Thr AGC TCG Ser ATG TAC Met	AGC TCG Ser AGC TCG Ser AAA TTT Lys	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val	GAC CTG Asp CTT GAA Leu 750	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser	AAC TTG ASD 710 AAA TTT Lys	AGT TCA Ser AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TTT Lys> 0 * TCA AGT Ser> 720 * AAC TTG Asn>
AAT TTA ASD AAA TTT Lys GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	CAA Val AAG TTC Lys 680 TTG AAC Leu 7	AAA TTT Lys CAA GTT Gln CCT GGA Pro	GAG CTC Glu 64 AAT TTA ASN GGT CCA Gly	GAA Leu  O GTT CAA Val  690 GAA CTT Glu  GAT	TGT Thr AGC TCG Ser ATG TAC Met	AGC TCG Ser  AGC TCG Ser  AAA TTT Lys	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val	GAC CTG Asp CTT GAA Leu 750	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser	AAC TTG ASD 710 AAA TTT Lys 76	AGT TCA Ser AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG ASD>
AAT TTA ASD AAA TTT LyS GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	CAA Val AAG TTC Lys 680 TTG AAC Leu 7	AAA TTT Lys CAA GTT GIn CCT GGA Pro 30 AAG TTC	GAG CTC Glu 6 AAT TTA ASN GGT CCA Gly TAC ATG	GAA Leu  10 GTT CAA Val  690 GAA CTT Glu  GAT CTA	TGT Thr AGC TCG Ser ATG TAC Met 740 CTA GAT	AGC TCG Ser AGC TCG Ser AAA TTT Lys	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val	GAC CTG ASP CTT GAA Leu 750 ACA	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser GAC CTG	AAC TTG ASD TTT Lys AAG TTC	AGT TCA Ser * AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG ASD>
AAT TTA ASD AAA TTT LyS GTA CAT Val	TCA AGT Ser 630 CCT GGA Pro GAT CTA ASP	CAA Val AAG TTC Lys 680 TTG AAC Leu 7	AAA TTT Lys CAA GTT GIn CCT GGA Pro 30 AAG TTC	GAG CTC Glu 6 AAT TTA ASN GGT CCA Gly TAC ATG	GAA Leu  10 GTT CAA Val  690 GAA CTT Glu  GAT CTA ASP	TGT Thr AGC TCG Ser ATG TAC Met 740 CTA GAT	AGC TCG Ser  AGC TCG Ser  AAA TTT Lys  ATT TAA Ile	GGA Pro 550 * CTT GAA Leu 70 GTT CAA Val * GCA CGT Ala	GAC CTG Asp CTT GAA Leu 750 ACA TGT	GTG CAC Val GAG CTC Glu GTA CAT Val	GCA CGT Ala 660 AAA TTT Lys AGC TCG Ser GAC CTG	AAC TTG ASD TTT Lys AAG TTC	AGT TCA Ser * AGC TCG Ser GAA CTT Glu	CCA GGT Pro 67 GTT CAA Val AAA TTT Lys	TIT Lys> 0 * TCA AGT Ser> 720 * AAC TTG ASD>

#### B-31 OSP C/ B-31 OSP A/ B-31 OSP B FUSION

7	70			780			79	0 .		ε	300		•	810		
	•		•	•		•		•	•		•		•	•		•
															GGC	
															CCG	
	Lys	Cly	Thr	Ser	Asp	Lys	Asn	Asn	Gly	Ser	Gly	Val	Leu	Glu	Gly	Val>
	82	20		ε	30			840			85	50		8	360	
		•	•		*		•	•		•		•	•		•	
															CTA	
															GAT	
	Lys	Ala	Asp	Lys	Ser	Lys	Val	Lys	Leu	Thr	Ile	Ser	Asp	Asp.	Leu	Gly>
	-	870			88	30		ε	390			900			9;	.0
	•	•		•		•	•		•		*	•		•		•
															GTA	
															CAT	
	Gln	Thr	Thr	Leu	Glu	Val	Phe	Lys	Glu	Asp	Gly	Lys	Thr	Leu	Val	Ser>
		9	920			930			94	10		9	950			960
	•	•	•		•	•		•		•	•		•		•	•
	AAA	AAA	GTA	ACT	TCC	AAA	GAC	AAG	TCA	TCA	ACA	GAA	GAA	AAA	TTC	TAA
٠	TTT	TTT	CAT	TGA	AGG	TTT	CTG	TTC	AGT	AGT	TGT	CTT	CTT	TTT	AAG	ATT
	Lys	Lys	Val	Thr	Ser	Lys	Asp	Lys	Ser	Ser	Thr	Glu	Glu	Lys	Phe	Asn>
	•		9.	70		9	980		•	990			100	00		
		•		•	•		•		•	*		• '		•	•	
.,	GAA	AAA	GGT	GAA	GTA	TCT	GAA	AAA	ATA	ATA	ACA	AGA	GCA	GAC	GGA	ACC
	CTT	TTT	CCA	CTT	CAT	AGA	CTT	TIT	TAT	TAT	TGT	TCT	CGT	CTG	CCT	TGG
	Glu	Lys	Gly	Glu	Val	Ser	Glu	Lys	Ile	Ile	Thr	Arg	Ala	Asp	Gly	Thr>
10	10		:	1020			10:	30		10	040		1	1050		
	•		•	•		•		•	•		•		•	. •		•
	AGA	CTT	GAA	TAC	ACA	GGA	ATT	AAA	AGC	GAT	GGA	TCT	GGA	AAA	GCT	AAA
	TCT	"GAA	CTT	ATG	TGT	CCT	TAA	TTT	TCG	CTA	CCT	AGA	CCI.	TIT	'CGA	TIT
	Arg	Leu	Glu	Tyr	Thr	Gly	Ile	Lys	Ser	Asp	Gly	Ser	Gly	Lys	Ala	Lys>
	10	60		. 1	070		:	1080			109	90		1:	100	
		•	•		◆.		•	•		•		•	•		*	
	GAG	GTT	TTA	AAA	GGC	TAT	GTT	CTT	GAA	GGA	ACT	CTA	ACT	GCT	GAA	AAA
																TTT
	Glu	Val	Leu	Lys	Gly	Tyr	Val	Leu	Glu	GJA	Thr	Leu	Thr	Ala	Glu	Lys>
		1110			11.	20	•	1	130			1140			11	50
	•	•		•		•	•		•		•	•		•		•
															AAT	
	TGT	TGT	AAC	CAC	CAA	TTT	CTT	CCT	TGA	CAA	TGA	AAT	TCG	TTT	TTA	AAT
	<b>で</b> か~	Thr	T.en	Va1	Val	Lvs	Glu	Glv	Thr	Val	Thr	Leu	Ser	LVS	Asn	Ile>

FIGURE 31 (3 of 4)

B-31 OSP C/ B-31 OSP A / B-31 OSP B FUSION

1160 1170 1180 1190 1200

TCA AAA TCT GGG GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT AGT TTT AGA CCC CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA Ser Lys Ser Gly Glu Val Ser Val Glu Leu Asn Asp Thr Asp Ser Ser>

1210 1220 1230 1240

GCT GCT ACT AAA AAA ACT GCA GCT TGG AAT GAC AGT ACT AGC ACT TTA CGA CGA TGA TTT TTT TGA CGT CGA ACC TTA CTG TCA TGA TCG TGA AAT Ala Ala Thr Lys Lys Thr Ala Ala Trp Asn Asp Ser Thr Ser Thr Leu>

1250 1260 1270 1260 1290

ACA ATT AGT GCT GAC AGC AAA AAA ACT AAA GAT TTG GTG TTC TTA ACA TGT TAA TCA CGA CTG TCG TTT TTT TGA TTT CTA AAC CAC AAG AAT TGT Thr Ile Ser Ala Asp Ser Lys Lys Thr Lys Asp Leu Val Phe Leu Thr>

1300 1310 1320 1330 1340

GAT GGT ACA ATT ACA GTA CAA CAA TAC AAC ACA GCT GGA ACC AGC CTA CTA CCA TGT TAA TGT CAT GTT GTT ATG TTG TGT CGA CCT TGG TCG GAT ASP Gly Thr Ile Thr Vai Gln Gln Tyr Asn Thr Ala Gly Thr Ser Leu>

1350 1360 1370 1380 1390

GAA GGA TCA GCA AGT GAA ATT AAA AAT CTT TCA GAG CTT AAA AAC GCT CTT CCT AGT CGT TCA CTT TAA TTT TTA GAA AGT CTC GAA TTT TTG CGA Glu Gly Ser Ala Ser Glu Ile Lys Asn Leu Ser Glu Leu Lys Asn Ala>

1400

TTA AAA TAA AAT TTT ATT Leu Lys \*\*\*>

FIGURE 31 (4 of 4)

#### FUSION SEQUENCE

B-31 OSP A/ B-31 P-93 (1168-2100) Sequence Range: 1 to 1720

			10	•		20			3	0			40		
		,	•		•	•		•		•	-	•			•
ምም የሌላ	1G C#	יירי דיי אר אט	IT GI	T AG	C AG	CCT	I GA	C GA	G AA	A A	AC AC	SC G2	T T	CA G	Ta gat
· ĸ					<b>U</b> 1 C	S GA	~ ~ 1		. 7-7		rc - <del>r</del> c	~~ ~:			
			•		3		ע	£	K	. 1	V 5	•	7 9	5 1	AT CTA J D>
50			6	0			70			80	L		,		
		•		•	•		•		•		,	_		90	•
TT	G CC	T GG	T GA	A ATO	S AA	GT1	CI	T G7.	A AG	C AA	A GA	A AA	а а	CAA	♣ LÀ GAC
				• • •	- 411		LIA	. (	rrc		~~	~ ~~			
	-	G	E	m	K	. <b>V</b>	L	V	S	K	E	K	N	K	T CTG
	100			110			120	1							
	•		•	•		. •		•			130		_	140	
GG	AA C	G TA	C GAT	CTA	ATT	. CCF	202		C N C		~ ~~		_	* *	
				, OV			161	CAT	. (77)	. T		· ~	~ ~·	•	
G	K	Y	D	L	I	, A	T	v	D	K	L	E	L	K	T CCT G>
	150				60										
. •	•	•	•		•	•		•		-	180				190
ACI	TCI	GAT	AAA 1	AAC	AAT	GGA	TCT	GGS		~~~			•		GCT
T	S	D	K	N	N	G	S	G	v	L	E	G	V	K	CGA A>
		200							•				•	••	~~
•		-		•	210		•	2				230			240
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B-31 OSP A/ B-31 P93

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FIGURE 32 (2 of 5)

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	• CAG GTC	coo ccc		GGA CCT	ATT TAA I	TAT ATA Y	GAA CTT	CGT GCA R	GAA CTT E	AAA TTT K	GAT CTA D	TTG AAC L	GTT CAA V	GTT CAA V	ATT	AAA TTT
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	CAG GTC Q ATG	CGG GCC R 1	ATA Y 400 TCA AGT S	GGA CCT G GGA CCT G	ATT TAA I AAA TTT	TAT ATA Y 1410 GCT CGA	GAA CTT E AAG TTC K	CGT GCA R CTT GAA L	GAA CTT E 14: CAG GTC Q	AAA TTT K 20 • ATA TAT I	GAT CTA D CTT GAA L	TTG AAC L 14 GAT CTA	GTT CAA V 130 AAA TTT K	GTT CAA V CTT GAA L	ATT TAA I GAA CTT	AAA TTT K> 1440 AAT
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	CAG GTC Q ATG TAC M	CGG GCC R 1 GAT CTA D AAA TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G SO GTA CAT V	ATT TAA I AAA TTT K TCA AGT S	TAT ATA Y 1410 CGA A 1 GAG CTC	GAA CTT E AAG TTC K 460 TCT AGA	CGT GCA R CTT GAA L AAT TTA N	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC	GAT CTA D CTT GAA L ATT TAA I	TTG AAC L 14 GAT CTA D AAT TTA N	GTT CAA V 130 AAA TTT K AAA TTT K	CTT CAA V CTT GAA L SO . AAT TTA N	ATT TAA I GAA CTT E TCA AGT S	AAA TTT K> 1440 AAT TTA N>
1	CAG GTC Q ATG TAC M TTA AAT L 490 CTT	CGG GCC R I GAT CTA D AAA TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G TA CAT V	ATT TAA I AAA TTT K TCA AGT S	TAT ATA Y 1410 GCT CGA A 1 GAG CTC E	GAA CTT E AAG TTC K 460 TCT AGA S 15	CGT GCA R CTT GAA L AAT TTA N 10	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC E 1	GAT CTA D CTT GAA L ATT TAA I 520 GCT	TTG AAC L GAT CTA D AAT TTA N GTT	GTT CAA V 130 AAA TTT K 141 AAA TTT K	CTT CAA V CTT GAA L 30 AAT TTA N 1530 GAT	ATT TAA I GAA CTT E TCA AGT S	AAA TTT K> 144C AAT TTA N> TCT AGA S>
	CAG GTC Q ATG TAC M TTA AAT L 490 CTT GAA	CGG GCC R 1 GAT CTA D AAA TTT K	ATA Y 400 TCA AGT S 14 GTG CAC V	GGA CCT G GGA CCT G TAT V 1500	ATT TAA I AAA TTT K TCA AGT S	TAT ATA Y 410 GCT CGA A 1 GAG CTC E AAA TTT	GAA CTT E AAG TTC K 460 TCT AGA S 15	CGT GCA R CTT GAA L AAT TTA N	GAA CTT E 14: CAG GTC Q TTT AAA F	AAA TTT K 20 ATA TAT I 1470 GAG CTC E 1 GTA CAT	GAT CTA D CTT GAA L ATT TAA I S20 CCT CGA	TTG AAC L 10 GAT CTA D AAT TTA N GTT CAA	GTT CAA V 130 AAA TTT K 141 AAA TTT K	CTT CAA V CTT GAA L 30 AAT TTA N 1530 GAT	ATT TAA I GAA CTT E TCA AGT S	AAA TTT K> 144C AAT TTA N> TCT AGA S>

B-31 OSP A/ B-31 P-93

1550 1560 1570 AGT AGT AAT GAT TGG AGA TTG GCC AAA TTT TCT CCT AAA AAT TTA GAT TCA TCA TTA CTA ACC TCT AAC CGG TTT AAA AGA GGA TTT TTA AAT CTA S S N D W R L A K F S P K N L D> 1600 1590 1610 1620 GAG TTT ATT CTT TCA GAG AAT AAA ATT ATG CCT TTT ACT AGC TTT TCT CTC AAA TAA GAA AGT CTC TTA TTT TAA TAC GGA AAA TGA TCG AAA AGA EFILSENKIMPFTSFS> 1640 1650 1660 1670 • GTG AGA AAA AAT TTT ATT TAT TTG CAA GAT GAG TTT AAA AGT CTA GTT CAC TCT TTT TTA AAA TAA ATA AAC GTT CTA CTC AAA TTT TCA GAT CAA V R K N F I Y L Q D E F K S L V> 1690 1700 1710 ATT TTA GAT GTA AAT ACT TTA AAA AAA GTT AAG GGT CAC C TAA AAT CTA CAT TTA TGA AAT TTT TTT CAA TTC CCA GTG G I L D V N T L K K V K G H X>

FIGURE. 32 (5 of 5)

B-31 OSP B/ B-31 P41 (122-234)

OSPB/Fla122-234

Sequence Range: 1 to 1180

20 30 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> - 60 \_ 80 \_\_\_ . 50 70 90 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q 110 120 140 • CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 200 220 210 230. GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A T I D Q V E L K G T S D K N N> 260. 270 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 310 - 320 300 . . . TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT

A S N Q K I S S K V T K K Q G S>

## B-31 OSP B/ B-31 P41 (122-234)

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FIGURE 33 (2 of 4)

## B-31 OSP B/ B-31 P41 (122-234)

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AC.	A GCT	r GG	A ACC	AGC	CTA	GAZ	. GGA	TC	A GC.	A AG	CAD 1	A ATT	נגג ז	AA:	r ctt
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TC	A GAG	CTI	AAA :	AAC	GCT	TTA	AAA	GGI	CAC	ccc	ATO	GCT	CAZ	TAT	AAC
WG 1	LIL	. 624	7 7.7.7.	116	CGA	AAT	TTT	CCA	GTO	3 666	: ጥልር	. CCP			-
5	E	L	K	N	A	L	K	G	H.	. P=	= = M =	A	Q	Y	N>
	870			8	80			890			900			_	
*	•	•	•		•			•		•	*			9	_
CAA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	GCI	TCT	CAA	AAT	GTA	) ACA	ACA
GII	IAC	610	TAL	AAT.	AGT	TTG	TTT	AGA	CGA	AGA	CTT	J-T	C 3 T	TOT	TGT
Q	M	H	М	L	S	. 17	K	S	A	S	Q	N	V		T>
		920			930			•							
•		•		•	930			9	40			950			960
GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	444	ערה ע -	220	303	~~`	•	
CGW			GAA	CCT	TAC	GTC	GGA	CGT	TTT	• ጥደል	TATE	مدتانك		-	
A	E	E	Ĺ	G	M	Q	P	A	K	I	N	T	P	LG1	AGT SS
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	•		•	•	•	•		•	990			100	00		
CTT	TCA	GGG	CTT	CAA	GCG	TCT	TGG	ACT	TTT.	AGA	تمنت	CAT		-	-
GAA	WOI		GAA	GTT	CGC	AGA	ACC	TGA	AAT	TCT	$C \lambda \lambda$	CTA	C > >	~~m	
L	s	G	L	Q	A	s	W	T	L	R	v	H	V	G	A >
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ACC	CAA				ATT	ĞСТ	GTA	ግ ጥፈል	ىلىنىڭ لا	4. A.		*	•		•
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T	Q	D	E	A	I	A	v	N	I	Y	A A	A	N N		
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AAT	CTT	علك	<del>ПСТ</del>	CCT.	CNC	- 	•	<b></b>	•		•	•		•	
TTA	CTT	AAG	AGA	CCA	CTC	CCT	CCI	CMM	ACT	GCT	CAG	GCT	GCA	CCG	GTT CAA
N	L	F	s	G	E	G	A	O.	TGA	CCA	GTC	CGA	CGT	eec.	CAA V>
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	1110			112	0		11	30		1	140			115	0
CAA	CNC		• •		•	•		*		•	•		•		_
CAA	GAG	CCA	CAN	CAA	CAG	GAA	GGA	GCT	CAA	CAG	CCA	GCA	CCT	GCT	ACA
Q	CTC	CCA	V	611	GIC	CTT	CCT	CGA	GTT	GTC	GGT	CGT	GGA	CGA	TGT
~	-	9	¥	¥	Q	E	G	A	Q	Q	₽	A	₽	A	T>

B-31 OSP B/ B-31 P41 (122-234)

GCA CCT TCT CAA GGC GGA GTT GGT CAC C
CGT GGA AGA GTT CCG CCT CAA CCA GTG G
A P S Q G G V G H X>

FIGURE 33 (4 of 4)

8-31 OSP B / B-31 P41 (122-295)
Sequence Range: 1 to 1363

20 30 10 GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT S I G S Q K E N D L> AQKGAE 50 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA-AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 100 110 120 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT AAT ARA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 210 200 220 230 GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA I D Q V E L K G T S D K N N> 250 260 270 GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT G S G T L E G S K P D K S K V K> 290 300 310 320 . • TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 340 360 ' 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT N Q K I S S K V T K K Q G S>

FIGURE 34 (1 of 4)

## B-31 OSP B / B-31 P41 (122-295)

390		400		4	10		,	20		
• · · · · ·	*	•	, •		_				•	430
ATA ACA C	FAG GAA A	CT CTC	AAA	GCT	AAT :	AAA '	TTA G	AC TCA	AAG .	AAA 777
TAT TGT C										
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44	0	450			460			470		
	•	•		. •			•			480
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TGT TCT A	יים או ה S או ה	T TGA 7	rgt (	GAA (	CTT A	TG: A	CT-C	TAT TA	TGT C	TA CGA
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	490	´ 50	00		5	10		۶-		-
CAC AAM O	*	•	•	•		_	•	52		•
GAC AAT GO	T ACA AA	A GCA G	TA C	SAA A	CI C	TA A	AA AA	T AGC	ATT 1	مبلت
CTG TTA CO										TC GAA
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530	540		550			560	<b>1</b>			•
· · ·	•	•	•		_		_		570	_
GAA GGA AG CTT CCT TC	T CTT GT.	A GTC G	GA A	AA A	CA AC	A G	rg ga	A ATT	AAA CX	A CCT
CTT CCT TC E G S	A GAA CA!	r cag c	CTT	TT T	GT TG	T C	CT CT	TAA	TTT CI	T CCA
- 0	L V	V (	ا ف	Κ . :	r T	<b>`</b> •	E	· I	K E	G>
580	590		6	00			610			
ACT CTT AC	• . •	•		•	•			. •	620	
ACT GTT ACT	CTA AAA	AGA GA	A A	rt ga	AA AA	A GA	T GGA	AAA G	TA AA	A GTC
TGA CAA TG				w ci	1 11	T CT	A CCT	J. L.L.L. L	'A T	
	- ~	. A E		L E	K	D	G	К	v K	V>
630	6	40		650			660	•		
TTT MMC	•	*	•	_		•				70
TTT TTG AAT	GAC ACT	GCA GG	T TC	T AA	C AAJ	AA A	A ACA	GGT A	AA TGO	243
AAA AAC TTA F' L' N'	D T	CGT CC	A AG	ATT	G TTI	TT	TGT	CCA T	TT ACC	CTT
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680		690		. •	700		•	710		
GAC ACT ACT	*	•	•		•	•			•	720
GAC AGT ACT	TCG TCA	TTA ACA	A AT	T AG	r GCT	GAC	AGC	AAA AA	A ACT	AAA
CTG TCA TGA	S T	AAT TGT	TAL	A TC	A CGA	CTG	TCG	TIT TI	TT TGA	TTT
D S T		•	_	5	A	ט	S	K I	T	K>
	30	740	-		750	i		760		
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GAT TTG GTG CTA AAC CAC	AMG AMD	ACA GAT	, GG	R ACA	ATT	ACA	GTA	CAA CA	A TAC	AAC
CTA AAC CAC D L V	F L	TOT CTA	CC	TGI	TAA	TGT	CAT	GIT GI	T ATG	TTG
- •		1 D	G	T	I	T	V	Q Q		N>

FIGURE 34 (2 of 4)

#### B-31 OSP B / B-31 P41 (122-295)

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T	GT	CGA	CCT	TGG		GAT							TAA	TII	TTA	GAA
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		870			8	80		1	390		•	900			9	16
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C	AA	ATG	CAC	ATG	TTA	TCA	AAC	AAA	TCT	GCT	TCT	CAA	AAT	GTA	AGA	ACA
G.	TT	TAC	GTG	TAC	AAT	AGT	TTG	TTT	AGA	CGA	AGA	GTT	TTA	CAT	TCT	TGT
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						CGC						CAA	GTA	CAA	CCT	CGT
1	L	S	G	L	Q	A	S	W	T	L	R	V	H	v	G	A>
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TC	GG	GTT	CTA	CTT	CGA	TAA	CGA	CAT	TTA	TAA	ATA	CCT	CCI	ALY VAL	CYY	CCA
		Q	D	E	A	I,	A	v	N	I	Y	A	A	N	v	A>
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A.	AT	CII	TTC	TCT	GGT	GAG	GGA	GCT	CAA	ACT	GCT	CAG	GCT	GCA	CCG	GTT
1.	1 W	GAA	AAG	AGA	CCA	CTC	CCT	CGA :	GTT	TGA	CGA	GTC	CGA	CGT	GGC	Cll
r	N	ملا	r	5	G	E	G	Α	Q	.Т	A	Q	A	A	P	V>
															•	
	1	110			112	20		11	30		4	130			, , -	. ^
•	1	110		•	112	•	•	11	.30		. 1	140		•	115	
* C2		•				•			•			140 -				•
G?	AA TT	GAG CTC	GGT CCA	GTT CAA	CAA GTT		GAA CTT	GGA CCT	GCT CGA	CAA GTT	CAG	CCA GGT	GCA CGT	CCT	GCT CGA	ACA TGT

FIGURE: 34 (3 of 4)

### B-31 OSP B / B-31 P41 (122-295)

	•••	<del></del>	•														
	1160				1170			1	180		1190				1200		
•		•		•	•	•	•		•	•	•	•		•	•		
GCA	CCT	TC	CA	A GGC	GG	A GT7	AA 1	r TC	r cc	r GT7	CAA 1	GT	ו אכו	AC	r aca		
CGT	GGA	AGA	GT	I CCC	CC	r car	TT/	A AG	A GG	A CA	TTA	A CAR	1 76.	TG	A TGT		
A	P	S	Q	G	G	V	N	S	P	V	N	V	T	T	<b>T</b> >		
•	1210				1220			1230			1240						
	*		•		•	•		•			•				•		
GTT	GAT	GC1	AA 1	r aca	TC	A CTI	GC	גג ז	TA A	GA.	TAA A	GCI	` AT?	` AG	ATG		
CAA	CTA	CGA	TŢ	A TGI	AG:	r gað	CG2	IT.	LAT 1	CTI	ATT :	CGA	TA	TC	TAC		
v	D	A	N	T	s	L	A	K	I.	E.,	N.	A	I	R	M>		
1250 1260						270		1280			1254						
•		* 1	•		•		•			•		•					
ATA A	AGT	GAT	CAA												•		
TAT :	TCA	CTA	GTT	TCC	CGT	TTA	TAA	CCF	CCY	770	CAA	AAT	AGA	CTT	GAA		
I	S	D	Q	R	A	N	L	G	A	F	011	M	1(7)	GAA	CIT		
*															£>		
1300			1:	310		1	320			133	1330			1340			
		•		•		•	•		*		•			•			
TCT A	ATA	AAG	TAA	AGT	ACT	GAG	TAT	GCA	ATT	GAA	AAT	CTA	AAA	GCA	TCT		
AGA 1	TAT	TTC	TTA	TCA	TGA	CTC	ATA	CGT	TAA	CTT	TTA	CAT	خنب	CCT	202		
S	I	K	N	S	T.	E	Y	A	I	E	N	L	K	Α	S>		
1350			1360											1			
•																	
TAT C	CT	CAA	ATA	GGT	CAC	С											
ATA C																	
••		_	_	_													

FIGURE 34 (4 of 4)

B-31 OSP B/ B-31 P41 (140-234) Sequence Range: 1 to 1141

				10			20			30			40			_		
	GC	A CA	LAA A	A GGT	r GC	C GAC	TCA	AT:	r GG:	TC	T CA	A AA:	A GA	<b>3</b> 3 4	T (3)	T CT		
	CO 1	. 611			4 66/	1 616	- AGI	TA	A CCX	A AC	<b>کری ک</b>	ملحك ملا	T (7)	نحمه ر	1 ~m			
	λ	Q	K	G	Α	E	S	I	G	S	Q	K	E	N	D	A GAT		
•	50			60				70			80			9	0			
			, C7 5			י אכים א					•		•		•	•		
	TTG	GAA	CTI	CTO	AGA	TCA	ىلىنىڭ بىرىن		1 107	CA	CAZ	AA. A	GCT	נגגיז	A CA	A GAC I CTG		
	Ŋ	L	E	D	s	S	ĸ	к	S	н	Q	N	A A	X TT	r GT: Q	T CTG D>		
100		. 110					ı	,		120								
		•	•		. •		•	•		•		•	. •	,	_			
	CTT	CCT	. GCG	GTG	ACA	GAA	GAC	TCA	್ರಾ	707	المناسف ر	-			CAA	<b>A</b> AA 1		
	~, ~,	COA					1110	A(27)		, y — y								
	_	•	•	•	•	L		5	V	S	L	F	N	G	N	X TTT K>		
150					160			170				180	180			190		
	*	*		•		•	. •		•		*	•		•				
	AAT	AAA	CAT	AGC	AAA	GAA	AAA	AAT	AGC	TCC	GGC	AAA	TAT	GAT	KTT.	AGA		
	I	F	V	S	K	CII	K	TTA M	TCG	AGG	CCG	TTT	ATA	CTA	LAA	Y AGY		
					••			14			G	K	Y	D	L.	R>		
	200			210			•				230				24:			
	GCA	202	אדים	CAT	CAC	~~~~ *		*		•	•		•		_			
	CGT	TGT	TAA	CTA	GTC	CAA	CTT	CIT	AAA	GGA	ACT	TCC	GAT	AAA	AAC	AAT TTA		
	A	T	I	D	Q	v	E	L	K	CCI	TGA T	AGG	CTA	TIT	TTG	TTA ×X		
								_	••			3		K	N	N >		
*		250		260			•		270		21	_						
	GGT	TCT	GGA	ACC	CTT	GAA	GGT	TCA	244	CCT	CNC	*	A CT	* * * * * * * * * * * * * * * * * * * *	-	AAA.		
	~~.	11011	~~ .	100	OW.		CLA	ACTI	ساست	CCA			-		CAT	AAA TTT		
	G	S	G	T	L	E	G	S	K	P	D	K	s	к		K>		
2	90			300			31	.0		:	320			330				
	•		•			•	<u>د</u> د	•	•		*		•			•		
	TTA	ACA	GTT	TCT	GCT	GAT	TTA	AAC	ACA	GTA	ACC	TTA	GAA	GCA	TTT	GAT		
				ひらひ	COV	LIM	AAT	1-14.3	TIT	ידימי	TOO	2 2 00						
	_	•	•	3	^	ט	ب	N	T	V	T	L	E	Α	F.	CTA D>		
340		350								37								
	GCC	٠ ۲	- 2 2 C	C 3 2	* * * * * * * * * * * * * * * * * * * *	3 000	*	•		*		•	•					
	CGG	TCG	TTG	CAA GTT	ተተተ ተ	ATT TAB	TCA	AGT	AAA	GTT	ACT	AAA	AAA	CAG	GGG	TCA		
	A	s	N	0	K	I	AG I	CA	TTT	CAA	TGA	TTT	TTT	GTC	CCC	TCA AGT S>		
				-		-	. –	J	I.	•	Τ.	<i>L</i>	K	Q	G	S>		

#### B-31 OSP B/ B-31 P41 (140-234)

	390			4	00			410		•	420			4	30
•	•		•		•	•		•		*			•		•
					CTC GAG										
					L										
	,												••		
•	- (	440	•	•	450		•	4		•		470		•	480
ACA	AGA	TCA	AAC	GGA	ACT	ACA	CTT	GAA	TAC	TCA	CAA	ATA	ACA	GAT	
TGT	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
<b>T</b>	R	S	N	G.	T	T	L	E	Y	S_	Ω.,	I	T	D	À>
		49	90	·	5	500			510			5:	20		
	•		•	•		•		•	•		•		•	•	
GAC	TAA	CGA	ACA	AAA	GCA CGT	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CII
D	N	A	T	K	A	. V	E	T	L	K	N	S	TAA	TTC K	لائمة ح آ
										•	٠.			••	-
530		•	540	-	•	. 55	50			560		•	570		•
GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
CTT	CCT	TCA	GAA	CAT	CAG	CCT	TTT	TGT	TGT	CAC	CTT	TAA	TTT	CTT	CCA
•	G	S	.L	V	V	G	K	T	T	V	Ε	I	K	Ε	G>
<sup>®</sup> 58	30		9	590			600		•	6:	10		. 6	520	
58	•	•		•		*	•				*	•		•	
ACT	GTT	ACT TGA	CTA	AAA	AGA	⋆ GAA	ATT	GAA	AAA	GAT	• GGA	* AAA	GTA	AAA	GTC
ACT TGA	GTT CAA	TGA	CTA GAT	AAA TTT	TCT	GAA CTT	TTA	GAA CTT	AAA TTT	GAT CTA	• GGA CCT	AAA TTT	GTA CAT	AAA TTT	CAG
ACT TGA	GTT CAA V	TGA T	CTA GAT	AAA TTT K	TCT R	GAA CTT	ATT TAA I	GAA CTT E	AAA TTT K	GAT CTA D	GGA CCT G	AAA TTT K	GTA CAT V	AAA TTT K	CAG V>
ACT TGA	GTT CAA	TGA T	CTA GAT	AAA TTT K	TCT	GAA CTT	ATT TAA I	GAA CTT	AAA TTT K	GAT CTA D	• GGA CCT	AAA TTT K	GTA CAT V	AAA TTT	CAG V>
ACT TGA T	GTT CAA V 630	TGA T AAT	CTA GAT L GAC	AAA TTT K 64	TCT R 10 • GCA	GAA CTT E	ATT TAA I	GAA CTT E 50	AAA TTT K	GAT CTA D	GGA CCT G 660	AAA TTT K	GTA CAT V	AAA TTT K 67	CAG V>
ACT TGA T	GTT CAA V 630 TTG AAC	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 • GCA CGT	GAA CTT E GGT CCA	ATT TAA I TCT AGA	GAA CTT E 550 AAC TTG	AAA TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC	CAG V> O GAA CTT
ACT TGA T	GTT CAA V 630 TTG AAC	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 • GCA	GAA CTT E GGT CCA	ATT TAA I TCT AGA	GAA CTT E 550 AAC TTG	AAA TTT K AAA TTT	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC	CAG V> O GAA CTT
ACT TGA T	GTT CAA V 630 TTG AAC L	TGA T AAT TTA	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA	TCT R 10 GCA CGT A	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	GAA CTT E 50 AAC TTG N	AAA TTT K AAA TTT K	GAT CTA D	GGA CCT G 660 ACA TGT	AAA TTT K GGT CCA	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N	CTA GAT L GAC CTG	AAA TTT K 64 ACT TGA T	TCT R 10 GCA CGT A	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	GAA CTT E 550 AAC TTG N	AAA TTT K AAA TTT K	GAT CTA D * AAA TTT K	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G	GTA CAT V AAA TTT	AAA TTT K 67 TGG ACC W	CAG V> O GAA CTT E>
ACT TGA T TTT AAA F	GTT CAA V 630 TTG AAC L	TGA T AAT TTA N 580 ACT	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T	TCT R 10 GCA CGT A 690	GAA CTT E GGT CCA G	ATT TAA I TCT AGA S	GAA CTT E 550 AAC TTG N 70	AAA TTT K AAA TTT K	GAT CTA D AAA TTT K	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W _	CAG V> O GAA CTT E> 720
ACT TGA T TTT AAA F GAC CTG	GTT CAA V 630 TTG AAC L AGT TCA	TGA T AAT TTA N 580 ACT TGA	CTA GAT L GAC CTG D	AAA TTT K 64 ACT TGA T ACT TGA	TCT R 10 GCA CGT A	GAA CTT E GGT CCA G	ATT TAA I CT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G 10 AAA TTT	GTA CAT V AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 0 GAA CTT E> 720 AAA
ACT TGA T TTT AAA F GAC CTG	GTT CAA V 630 TTG AAC L AGT TCA	TGA T AAT TTA N 580 ACT TGA	CTA GAT L GAC CTG D AGC TCG	AAA TTT K 64 ACT TGA T ACT TGA	TCT R GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT	ATT TAA I CT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K GCT CGA A	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K  GGT CCA G 10 AAA TTT K	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 0 GAA CTT E> 720 AAA
ACT TGA T TTT AAA F GAC CTG	GTT CAA V 630 TTG AAC L AGT TCA	TGA T AAT TTA N 80 ACT TGA T	CTA GAT L GAC CTG D AGC TCG	AAA TTT K 64 ACT TGA T ACT TGA	TCT R GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G	ATT TAA I CT AGA S ATT TAA	GAA CTT E 550 AAC TTG N 70 AGT TCA	AAA TTT K AAA TTT K	GAT CTA D AAA TTT K GAC CTG	GGA CCT G 660 ACA TGT T	AAA TTT K GGT CCA G 10 AAA TTT	GTA CAT V AAA TTT K AAA TTT K	AAA TTT K 67 TGG ACC W ACT TGA	CAG V> 0 GAA CTT E> 720 AAA
ACT TGA T TTT AAA F GAC CTG D	GTT CAA V 630 TTG AAC L AGT TCA S	TGA T AAT TTA N 80 ACT TGA T GTG	CTA GAT L GAC CTG D AGC TCG S	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R 10 GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TCT AGA S ATT TAA I	GAA CTT E 50 AAC TTG N AGT TCA S	AAA TTT K AAA TTT K GCT CGA A 750	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	AAA TTT K  GGT CCA G  10 AAA TTT K  76 CAA	GTA CAT V AAA TTT K AAA TTT K CAA	AAA TTT K 67 TGG ACC W ACT TGA T	CAG V> 0 GAA CTT E> 720 AAA TTT K>
ACT TGA T TTT AAA F GAC CTG D	GTT CAA V 630 TTG AAC L AGT TCA S TTG AAC	TGA T AAT TTA N 80 ACT TGA T GTG CAC	CTA GAT L GAC CTG D AGC TCG S 10 AGC AAG	AAA TTT K 64 ACT TGA T ACT TGA T	TCT R GCA CGT A 690 TTA AAT L	GAA CTT E GGT CCA G ACA TGT T	ATT TAA I TCT AGA S ATT TAA I GGT CCA	GAA CTT E 50 AAC TTG N AGT TCA S	AAA TTT K AAA TTT K GCT CGA A 750 ATT	GAT CTA D AAA TTT K GAC CTG D	GGA CCT G 660 ACA TGT T AGC TCG S	AAA TTT K  GGT CCA G 10 AAA TTT K  76 CAA GTT	GTA CAT V AAA TTT K AAA TTT K CAA	AAA TTT K 67 TGG ACC W ACT TGA T TAC ATG	CAG V> 0 GAA CTT E> 720 AAA TTT K>

FIGURE 35 (2 of 3)

### B-31 OSP B/ B-31 P41 (140-234)

																•
770	1			780					•					810	)	
•	•	•	•	•		•				· .			• .	•	•	•
AC	A GC	TC	GA	ACC	AGC	CTA	. GAA	GGA	TCA	GC?	AG:	r GAJ	ATT	LAA 1	AAT	CII
TG	T CG	A C	CT	TGG	TCG	GAI	, CII	CCI	, AGI	, CGI	TC	CTT	TAZ	י דידי	لابلت	CAA
T	A	•	G	T	S	Ĺ	Ε	G	S	.A	s	Ε	I	K	N	L>
													_	• • • • • • • • • • • • • • • • • • • •	• • •	
	820				830			840			8	350			860	
	, , <b>e</b>		•		•		•	•		*		•			_	
TC	A GA	GC	TT	AAA	AAC	GCT	TTA	AAA	GGT	CAĊ	ccī	ĀTĆ	GCT	T-T	C	AAT
AG	T CT	CG	AA	TTT	TTG	CGA	AAT	TTT	CCA	GTG	GGG	ፐልር	CCY	101	CTT	TTA
s	E		L	K	N	A	L	K	G	н	P	M	. CO.	. הטת	Q	IIA
									_	••	•	••	^	. 3	Q	14>
	87	0		•		80			890			900			٥	10
•		*		•										•		
GT	A AG	A A	.CA	GCT	GAA	GAG	CTT	GGA	ATG	CAG	CCT	GCA	444	<u>አ</u> ጥጥ	220	A C A
CA	I TC	1. 1.	GT	CGA	CTT	CTC	GAA	CCT	TAC	GTC	GGA	CGT	TTT	TAA	TTC	TOT
v	R		T	A	E	E	L	G	М	0	P	A	ĸ	т.	N	701
													••	•		
		92	0			930			9	40			950		•	960
•	•		*		•	•		•		•	*		•		•	•
CC	A GC.	A T	CA	CTT	TCA	GGG	CTT	CAA	GCG	·TCT	TGG	ACT	TTA	AGA	GTT	CAT
GG.	r. CG	I A	GT	GAA	AGT	CCC	GAA	GTT	CGC	AGA	ACC	TGA	AAT	TCT	CAL	CTA
P	A		S	L	S	G	L	Q	Α.	S	W	T	L	R	v	H>
				0			980			990			100	00		
	• • •			•	•				•	*	•	*		•	· •	
GII		A GO	CA	ACC	CAA	GAT	GAA	GCT	ATT	GCT	GTA	AAT	ATT	TAT	GCA	GCT
CAA		ı C	G.T.	TGG	GTT	CTA	CTT	CGA	TAA	CGA	CAT	ATT	AAT	ATA	CGT	CGA
V	G	4	A	T	Q	D	Ε	A	I	A	V,	N	· I	Y	A	A>
1010						•										
1010		*	. 1	020			103	-		10	040		3	.050		
227	י כחיו	c Gr	۸-	እ እጥ									•	<del>*</del> .		•
TTA	CAR		با مدت	ע עע ע דיטיט	CII	NAC.	101	CCI	GAG	GGA.	GCT	CAA	ACT	GCT	CAG	GCT
N	v		<u>.</u>	N	JAA	WWG	AGA	CCA	CTC	CCT	CGA	GTT	TGA	CGA	GTC	CGA
	•	•	<b>.</b>	44		E.	. <b>.</b>	G	£	G	A	Q	T	A	Q	A>
10	60			10	70		1	080			100					
	•		•		•			•		•	109	*		_	.00	
GCA	ccc	G:	TT (	CAA	GAG	GGT	GTT	CAA	CAG		CCN	-	~ .		•	GCA
CGI	, GGC	: C	AA (	GTT	CTC	CCA	CAA	GTT	GTC	CUT	CCT	GCI	CAA	CAG	GGT	GCA
Α	P	1	J	0	E	G	v	0	010	CII	CCI	COA	GIT	GIC	GGT P	CGT
					_	_	•	*	¥	<b>-</b>	G	A	Q	Q	P	A>
	1110	)			112	0		- 11	30		4	.140				
	•				•	*	•		•		•	•				
CCI	. GCI	` AC	CA	GCA	CCT	TCT	CAA	GGC	GGA	GTT	GGT	CAC	٠.			
GGA	CG	T	ST (	CGT	GGA	AGA	GTT	CCG	CCT	CAA	CCF	CAC	G.			
P	À	7	r	A	P	s	Q	G	G	v	G	H	X>			
							_	_	_	•	•	44	~>			

FIGURE 35 (3 of 3)

B-31 OSP B/ B-31 P41 (140 -295)

Sequence Range: 1 to 1324

10 20 30 -GCA CAA AAA GGT GCT GAG TCA ATT GGT TCT CAA AAA GAA AAT GAT CTA CGT GTT TTT CCA CGA CTC AGT TAA CCA AGA GTT TTT CTT TTA CTA GAT A Q K G A E S I G S Q K E N D L> 50 60 70 80 AAC CTT GAA GAC TCT AGT AAA AAA TCA CAT CAA AAC GCT AAA CAA GAC TTG GAA CTT CTG AGA TCA TTT TTT AGT GTA GTT TTG CGA TTT GTT CTG N L E D S S K K S H Q N A K Q D> 110 100 120 130 CTT CCT GCG GTG ACA GAA GAC TCA GTG TCT TTG TTT AAT GGT. AAT AAA GAA GGA CGC CAC TGT CTT CTG AGT CAC AGA AAC AAA TTA CCA TTA TTT L P A V T E D S V S L F N G N K> 150 160 170 180 ATT TTT GTA AGC AAA GAA AAA AAT AGC TCC GGC AAA TAT GAT TTA AGA TAA AAA CAT TCG TTT CTT TTT TTA TCG AGG CCG TTT ATA CTA AAT TCT I F V S K E K N S S G K Y D L R> 220 230 200 210 • GCA ACA ATT GAT CAG GTT GAA CTT AAA GGA ACT TCC GAT AAA AAC AAT CGT TGT TAA CTA GTC CAA CTT GAA TTT CCT TGA AGG CTA TTT TTG TTA A TIDQVELKGTSDKN N> 250 260 270 280 . • GGT TCT GGA ACC CTT GAA GGT TCA AAG CCT GAC AAG AGT AAA GTA AAA CCA AGA CCT TGG GAA CTT CCA AGT TTC GGA CTG TTC TCA TTT CAT TTT T L E G S K P D K S K V K> 290 300 . 310 320 330 TTA ACA GTT TCT GCT GAT TTA AAC ACA GTA ACC TTA GAA GCA TTT GAT AAT TGT CAA AGA CGA CTA AAT TTG TGT CAT TGG AAT CTT CGT AAA CTA L T V S A D L N T V T L E A F D> 350 360 370 GCC AGC AAC CAA AAA ATT TCA AGT AAA GTT ACT AAA AAA CAG GGG TCA CGG TCG TTG GTT TTT TAA AGT TCA TTT CAA TGA TTT TTT GTC CCC AGT A S N Q K I S S K V T K K Q G S>

FIGURE 36 (1 of 4)

## B-31 OSP B/ B-31 P41 (140 -295)

	4	390		_	. 4	00			410			42	0			430
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	TAT	TGT	CTC	י כאט	TO TO	CTC	AAA:	GCI	AA:	LAA 1	A TT	A GA	CTC	A AA	G AA	A TTA
	I	T	E	E	T	. GAC	K	A	N	t II.	ı AA:	r. C.L.	G AG	TTT	C TT	T AAI L>
	•					_	••	••	• • •	*		U	۵	K	K	L>
	-		440			450				160			470			480
	. ACA	) ACA	* TC3	3.3.0		٠,		•		•			•		•	
	TGT	TCT	AGT	י אאני י איז	CCT	TCA	· ACA	CTI	GA.	ATAC	TC	CA	A ATA	A AC	A GA	* T GCT A CGA
	T	R	s	N	G	T	T	L	E	Υ. Υ.	- C		TA:	r TG	r CT	A CGA A>
							_	_	_	•		Q	_	1	ט	A>
		_	4	90			500			510	)		5	520 É		
	C A C	አአጥ		301	•		*		•	•		•		•	•	•
	CTG	TTA	CGA	TGT	AAA TTT	CCT	GTA	GAA	ACT	CTA	AAA	LAA	AGC	ATI	AAC	G CTT
	Ð	N	A	T	ĸ	A	V	E	I GA	GAT	TTT	TTA N				
								_	•	_	A	14	5	I	K	L>
	530		_	540			5	50			560			570		
	GAA	GGA	AGT	C.T.T.	CTA	- TC		•	*		•		*	•		•
	CTT	CCT	TCA	GAA	CAT	CAG	CCT	AAA	ACA	ACA	GTG	GAA	ATT	' AAA	GAA	GGT
	E	G	S	L	v	v	G	ĸ	T	T	V	E	TAA	TTT	CII	CCA G>
											·	-	_	ν,	£	G>
	58	<b>5</b> ∪	•		590		_	600			6	-			620	
	ACT	GTT	ACT	CTA	AAA	AGA	GAA		CAA	* * * * * * * * * * * * * * * * * * * *	C > m		•			
	TGA	CAA	TGA	GAT	TTT	TCT	CTT	TAA	CTT	TTT	CTA	CCT	AAA	GTA	AAA	GTC
	$\mathbf{T}$	V	T	L	K	R	E	I	E	К	D	G			K	
		630												·	••	. • -
	•	630	•	•	64		•	6	50		_	660			6	70
	TTT	TTG	AAT	GAC	ACT	GCA	GGT	TCT	220	<b>222</b>	*	٠ ۵ – ۲		*		•
	~~~	~~	IIA	C16	IGA	CG.T.	CCA	AGA	TTG	TTT	TTT	エピエ	CCA	ملململه	TGG	GAA
	F	L	N	D	T	A	G	s	N	K	, K	T	G	ĸ		· E>
			80			690										
	•		•		•	•		•	70	<b>*</b>		7	710			720
	GAC .	agt	ACT	AGC	ACT	TTA	ACA	ATT	AGT	GCT	GAC	AGC	444	222	*	* :
	~~~	* ~~~	100	166	LOA	AAT	.141.	ממידי	ערא	$\sim$		-				AAA TTT
	Ð	S	T	S	T	L	T	I	S	A	D	s	K	ĸ	T	TTT K>
		•		0			40									
		•		•	•		•		•	•		٠	7€		_	
	GAT '	TTG	GTG	TTC	TTA	ACA	GAT	GGT	ACA	ን ፈካሊ	3 C 3	CT.	~		ተል 🕝	AAC
-			-n-	$\sim$	w	וטו	LIA	( 'C 'A	ידיבויני	ממידי	AL	~ N M	~~~			
	ט	L	V	F	L	T	D	G	T	I	T	v	Q	Q	Y	N>

FIGURE 36 (2 of 4)

#### B-31 OSP B/ B-31 P41 (140 -295)

	770			78	0		•	790			800	V				-
	•		•		•	•		•		•					10	_
	AC.	A GC	T GG	A AC	C AG	CT	A GA	A GG	A TC	A GO	A AG	T GA	A AT	י ב	י א א	T CI
	10	1 66	4 .CC	ى د د.	G TU	J GA:	r CL	r cc	r ag	T CG	T TC	A CT	ጥ ጥኔ	A 7	~ ~	RT CT
	T	A	G	T	s	L	E	G	S	A	· S	E	I			L
	1	B20			830			840	)			850			860	
•		•		•	•		•	. •				•		•		
	TCA	A GAC	CT	T AA	A . AAC	GCI	ATT 1	LAA A	GG'	r ca	c cc	C AT	G GC	T TC	T CA	A AAT
	70.	E	- GA	~ 11	1 116	عمال د	L.AA.I		, CC	A CT.		~ ~ ~ .				
	J		ט		N	A	1	K	G	н	P	M	Α	S	Q	T TTA <n< td=""></n<>
		870	)		8	80			890			906	n			•
	•	•		•		*	•		•		•			•		910
	GTA	AGA	AC.	A GC	r GAA	GAG	CTŢ	GGA	ATC	CA	cc:	r GC	A AA	A AT	T AA	· C ACA
·				•	, C11		- GAA	CCT		יידים י		~~~	^~~	~ ~ .		_
	V	K	T	Α.	E	E	L	G	M	Q	P	A	K	I	N	G TGT T>
			9 <b>2</b> 0			930			. 9	40			950			
	*		•		•	•		*		•	•	,				960
	CCA	GCA	TC	CTI	TCA	GGG	CTT	CAA	GCG	TCI	TGG			AG:	יינים א	· CAT
			701	, Gran	, wer	CCC	GAA	GI.I.	CGC	AGA	ACC	TGA	AAT	TC	CAR	CAT A GTA
	P	A	S	L	s	G	L	Q	A	S	W	T	L	R		H>
			g	70			980			000					•	
		•		*	•		•	•	•	990				00	_	
(	GTT	GGA	GCA	ACC	CAA	ĠAT	GAA	GCT	ATT	GCT	GTA	ል አጥ	λΤΤ	- ተአጥ		GCT
(	·· · ·	CCI	ĻG.	100	GII	CIA	C1.1	CGA	TAA	CGA	САТ	TTA	TAA	ATA	CCT	GCT CGA
	٧	G	A	T	Q	D	·E	A	I	A	v	N	I		A	
10:	10			1020			103						•			
	•		•	•		•		•			040		_	1050		
,	TAA	GTT	GCA	AAT	CTT	TTC	TCT	GGT	GAG	GGA	GCT	CAA	) (T	~~~	~	•
•		Cius	CG 1	117	GAA	MAG	AGA	CCA	CIC	CCT	CGA	CTT	TC A	CGA	CTC	~~ `
	N	- <b>V</b>	A	-N	-L	F	S	G	E	G	A	Q	T	A	0	A>
	106	0		1	070										-	
		•	•		•		•	.080		•	109	_	_		100	
C	CA	CCG	GTT	CAA	GAG	GGT	GTT	CAA	CAG	GAA	GC A		CAA	C) C	. •	
	A	P	V	Q	E	G	V	Q	٠.٥	E	G	A	Q	Q	P	A>
		110										•		-	_	•••
•		+		•	112	*	♠.	11	30		. 1	.140			119	
C	CT	GCT	ACA	GCA	CCT	TCT	CAA	ccc	CCA	CTT		-		•		•
_	~			COI.	SOM	~~	G1"1"	CTT	سب	C > N	A LLD.	101	~			
	P	A	T	Α	P	S	Q	G	G	V	N	S	D D	UAA V	TTA	CAA V>
										-		_	2	٧	N	V > _

FIGURE 36 (3 of 4)

### B-31 OSP B/ B-31 P41 (140 -295)

	1	160			1170			11	80		1	190			1200
•		•	•	•	•		•,		•					•	. •
ACA TGT	ACT TGA	ACA TGT	GTT CAA	GAT CTA	GCT CGA	AAT TTA	ACA TGT	TCA AGT	CTT GAA	GCT CGA	AAA	ATT	GAA	AAT	GCI
<b>T</b>	T <sub>.</sub>	T	v	D	A	N	T	S	L	A	ĸ	I	E		A>
		12:	10		1:	220			1230			12	6 D		
	•		•	•		•		•	•		•		•	•	
ATT	AGA	ATG	ATA	AGT	GAT	ĊAA	AGG	GCA	AAT	TTA	GGT	GCT	TTC	CÄÄ	ልኔጥ
TAA	TCT	TAC	TAT	TCA	CTA	GTT	TCC	CGT	TTA	AAT	CCA	CGA	AAG	GTT	TIL
I	R	М	I	s	D	Q	R	A	N	L	G	A	F		N>
1250		:	1260			127	70	-	15	280		•	260		
. •		•	•		•		•	•	12	•		•	1290		
. AGA	CTT	• GAA	TCT	ATA	<b>∔</b> AAG	AAT	* AGT	* ACT	GAG	TAT	GCA	<b>ب</b> للم	•	AAT	• CTA
AGA TCT	GAA	GAA CTT	TCT AGA	ATA TAT	AAG TTC	AAT ATT	* AGT TCA	ACT TGA	GAG CTC	TAT ATA	CGT	• ATT TAA	GAA CTT	AAT TTA	CTA GAT
AGA TCT	GAA	GAA CTT	TCT AGA	ATA	AAG TTC	AAT ATT	* AGT TCA	ACT TGA	GAG CTC	TAT	CGT	<b>ب</b> للم	GAA CTT	ATT	CTA GAT L>
AGA TCT	L	GAA CTT E	TCT AGA	ATA TAT I	AAG TTC	AAT TTA N	AGT TCA S	ACT TGA	GAG CTC	TAT ATA	CGT	• ATT TAA	GAA CTT	ATT	GAT
AGA TCT R	L DD	GAA CTT E	TCT AGA S	ATA TAT I	AAG TTC K	AAT TTA N	AGT TCA S	ACT TGA T	GAG CTC E	TAT ATA	CGT	• ATT TAA	GAA CTT	ATT	GAT
AGA TCT R 130	L DD GCA	GAA CTT E	TCT AGA S	ATA TAT I	AAG TTC K	AAT TTA N	AGT TCA S	ACT TGA T	GAG CTC E	TAT ATA	CGT	• ATT TAA	GAA CTT	ATT	GAT
AGA TCT R 130	L DD GCA	GAA CTT E TCT AGA	TCT AGA S 13 TAT ATA	ATA TAT I	AAG TTC K CAA GTT	AAT TTA N	AGT TCA S .320 .GGT CCA	ACT TGA T	GAG CTC E	TAT ATA	CGT	• ATT TAA	GAA CTT	ATT	GAT

FIGURE 36 (4 of 4)

Osp b/ fla (122-234) osp c Sequence Range: 1 to 1765

				LO		•	20		•	30				40		
		•		•	•		•		•	. •		•		• •	•	
				GGT												
	CGT	GTT	TTT	CCA									CTT	ΠA		
	A	Q	K	G	A	E	S	I	G	S	Q	K	E	X	, D	L>
	50			60			-	70			80			90		
	•		•	•		•		•	•		_•		•	•		•
				GAC.						•		• •				
				CTG												
	`N	L	E	D	S	S	.K	ĸ	S	H	Q	N	A	K	Q	D>
	10	00		1	110			120			1:	30			140	
		•	•		•		• '	•		•		•	•		•	
	CTT	CCT	GCG	GTG	ACA	GAA	GAC	TCA	GTG	TCT	TTG	TTT	AAT	GGT	AAT	AAA
	GAA	GGA	CGC	CAC											TTA	TTT
	L	P	A	v	T	Ε	D	S	V	S	L	F	N	G	K	K>
		150			16	50		1	170			180	•		19	5
	* ,	•		•		•	•		•		•	•		•		•
	TTA	TTT	GTA	AGC	AAA	GAA	AAA	AAT	AGC	TCC	GGC	AAA	TAT	GAT	TTA	AGA
	TAA			TCG										CTA	AAT	LÇI
	I,	F	V	S	ĸ	E	Κ -	N	5	S	G	K	Y	כ	L	₹>
		•	200	,		210	•		2:	20		2	30			240
								•		•	•		•		•	. •
	-		•			-										
				GAT												
	CGT	TGT	TAA	CTA	GTC	CAA	CTT,	GAA	TTT	CCT	TGA	ÀGG	CTA		TIG	TA
	CGT	TGT	TAA		GTC	CAA	CTT,	GAA	TTT	CCT	TGA	ÀGG	CTA		TIG	TA
	CGT	TGT	TAA	CTA	GTC	CAA V	CTT,	GAA	TTT	CCT	TGA	ÀGG	CTA	X.	TIG	TA
	CGT	TGT T	TAA I 2!	CTA D	GTC Q	CAA V	CTT E	GAA L	TTT K	CCT G 270	TGA T·	ÀGG S	CTA D	TTT K	TTG N	7.7A %>
	CGT	TGT T	TAA I 2! GGA	CTA D 50 *	GTC Q CTT	CAA V GAA	CTT E 260 • GGT	GAA L TCA	TTT K	CCT G 270 CCT	TGA T	ÄGG S • AAG	CTA D 28 AGT	TTT K SC AAA	TTG N • GTA	ATTA N>
	CGT A GGT CCA	TGT T TCT AGA	TAA I 2! GGA CCT	CTA D 50 ACC TGG	GTC Q CTT GAA	CAA V GAA CTT	E 60 GGT CCA	GAA L TCA AGT	TTT K AAG TTC	CCT G 270 CCT GGA	TGA T . GAC CTG	AGG S AAG TTC	CTA D 28 AGT TCA	TTT K S S AAA TTT	TTG N GTA CAT	ALA
	CGT	TGT T TCT AGA	TAA I 2! GGA CCT	CTA D 50 *	GTC Q CTT GAA	CAA V GAA CTT	E 60 GGT CCA	GAA L TCA AGT	TTT K AAG TTC	CCT G 270 CCT GGA	TGA T . GAC CTG	AGG S AAG TTC	CTA D 28 AGT TCA	TTT K S S AAA TTT	TTG N • GTA	ATTA N>
	CGT A GGT CCA	TGT T TCT AGA	TAA I 2! GGA CCT	CTA D 50 ACC TGG	GTC Q CTT GAA	CAA V GAA CTT	E E E E E E E E E E E E E E E E E E E	GAA L TCA AGT	TTT K AAG TTC	CCT G 270 CCT GGA P	TGA T . GAC CTG	AGG S AAG TTC	CTA D 28 AGT TCA	TTT K S S AAA TTT	TTG N GTA CAT	ALA
	CGT A GGT CCA G	TGT T TCT AGA	TAA I 2! GGA CCT	CTA D 0 50 ACC TGG T	GTC Q CTT GAA	CAA V GAA CTT	E E E E E E E E E E E E E E E E E E E	GAA L TCA AGT S	TTT K AAG TTC	CCT G 270 CCT GGA P	TGA T. GAC CTG D	AGG S AAG TTC	CTA D 28 AGT TCA	XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX	TTG N GTA CAT	ALA
	GGT CCA G	TGT T TCT AGA S	TAA I 2! GGA CCT G	CTA D 50 ACC TGG T 300 TCT	GTC Q CTT GAA L	CAA V GAA CTT E	CTT E 260 GGT CCA G 31	GAA L TCA AGT S	TTT K AAG TTC K	CCT GCT GGA P	TGA T. GAC CTG D	AGG S AAG TTC K	CTA D 28 AGT TCA S	ECA	TTG N GTA CAT V	N> AAA TTT K> GAT
	GGT CCA G 290 TTA	TGT T TCT AGA S	TAA I 2: GGA CCT G GTT CAA	CTA D 50 ACC TGG T 300 TCT AGA	GTC Q CTT GAA L GCT CGA	CAA V GAA CTT E GAT CTA	CTT E 260 GGT CCA G 3: TTA	TCA AGT S 10 * AAC	TTT K AAG TTC K ACA TGT	CCT G 270 CCT GGA P	GAC CTG D	AGG S AAG TTC K TTA AAT	CTA D 28 AGT TCA S GAA CTT	ECA CGCA CGT	TTG N GTA CAT V TTT AAA	N> AAA TTT K> GAT CTA
- 2	GGT CCA G 290 TTA	TGT T TCT AGA S	TAA I 2: GGA CCT G GTT CAA	CTA D 50 ACC TGG T 300 TCT	GTC Q CTT GAA L GCT CGA	CAA V GAA CTT E GAT CTA	CTT E 260 GGT CCA G 3: TTA	TCA AGT S 10 * AAC	TTT K AAG TTC K ACA TGT	CCT G 270 CCT GGA P	GAC CTG D	AGG S AAG TTC K TTA AAT	CTA D 28 AGT TCA S GAA CTT	ECA CGCA CGT	TTG N GTA CAT V TTT AAA	N> AAA TTT K> GAT CTA
	GGT CCA G TTA AAT L	TGT T TCT AGA S	TAA I 2: GGA CCT G GTT CAA V	CTA D 50 ACC TGG T 300 TCT AGA S	GTC Q CTT GAA L GCT CGA A	CAA V GAA CTT E GAT CTA D	CTT E 260 GGT CCA G 3: TTA AAT L	GAA L TCA AGT S 10 AAC TTG N	TTT K AAG TTC K ACA TGT	CCT G 270 CCT GGA P	GAC CTG D 320 ACC TGG	AGG S AAG TTC K TTA AAT	CTA D 28 AGT TCA S GAA CTT	AAA TTT E 330 GCA CGT A	TTG N GTA CAT V TTT AAA	N> AAA TTT K> GAT CTA
- 4	GGT CCA G TTA AAT L	TGT T TCT AGA S ACA TGT T	TAA I 2: GGA CCT G GTT CAA V	D  ACC TGG T  300  TCT AGA S	GTC Q CTT GAA L GCT CGA A	CAA V GAA CTT E GAT CTA D	CTT E 260 GGT CCA G 3: TTA AAT L	TCA AGT S AAC TTG N 360	AAG TTC K ACA TGT	CCT G 270 CCT GGA P GTA CAT V	GAC CTG D 320 ACC TGG T	AGG S AAG TTC K TTA AAT L	CTA D 28 AGT TCA S GAA CTT E	AAA TTT E 330 GCA CGT A	TTG N GTA CAT V TTT AAA F	N> AAA TTT K> GAT CTA D>
	GGT CCA G TTA AAT L 3	TGT T T AGA S ACA TGT T 40 AGC	TAA I 2: GGA CCT G GTT CAA V AAC	D 50 ACC TGG T 300 TCT AGA S	GTC Q CTT GAA L GCT CGA A	CAA V GAA CTT E GAT CTA D	CTT E 260 GGT CCA G 3: TTA AAT L	GAA L TCA AGT S 10 AAC TTG N 360	TTT K AAG TTC K ACA TGT T	CCT G 270 CCT GGA P GTA CAT V	GAC CTG D ACC TGG T 3.	AGG S AAG TTC K TTA AAT L	CTA D 28 AGT TCA S GAA CTT E	AAA TTT E 330 GCA CGT A CAG	TTG N GTA CAT V TTT AAA F	N> AAA TTT K> GAT CTA D>
	GGT CCA G TTA AAT L GCC CGG	TGT T T AGA S ACA TGT T AGC TCG	TAA I 2: GGA CCT G GTT CAA V AAC TTG	D  ACC TGG T  300  TCT AGA S	GTC Q CTT GAA L GCT CGA A 350	CAA V GAA CTT E GAT CTA D	CTT E 260 GGT CCA G TTA AAT L TCA AGT	GAA L TCA AGT S 10 AAC TTG N 360 AGT TCA	TTT K AAG TTC K ACA TGT T	CCT G 270 CCT GGA P GTA CAT V	GAC CTG D ACC TGG T ACT TGA	AGG S AAG TTC K TTA AAT L O AAA TTT	CTA D 28 AGT TCA S GAA CTT E AAA TTT	AAA TTT  E  GCA GCA CGT A  CAG GTO	TTG N GTA CAT V TTT AAA F 380 GGG CCC	N> AAA TTT K> GAT CTA D> TCA AGT

FIGURE 37 (1 of 5)

Osp b/ fla (122-234) osp c

		390			4	00			410			420				130
	•	•		•		•	•		•		•	. •		•		
	ATA	ACA	GAG	GAA	ACT	CTC	AAA	GCT	AAT	AAA	ŢTĀ	GAC	TCA	AAG	AA	ATTA
	IAT	TGT	E	E	TGA T	GAG L	TTT	CGA	TTA	TTI	, yyl	CTG	AG:			TAA 1
	-	•	۰		4		ν.	A	N	. K	L	D	S	K	K	L>
			440			.450			4	60			470			480
	•		•		•	•		*		•	•		•		•	_
	ACA	AGA	TCA	AAC	GGA	ACT	ACA	CII	GAA	TAC	TCA	CAA	ATA	ACA	GAT	CCI
	1.61	TCT	AGT	TTG	CCT	TGA	TGT	GAA	CTT	ATG	AGT	GTT	TAT	TGT	CTA	CGA
	•	Λ.	3	14	G	1	1.	L			S	Q	I	T	D	A>
			4.	90		,	500		•	510	±. 1.5 ·	•	5.	20		
		. •		•	•		•		•	•		•		•	•	
	GAC	AAT	GCT	ACA	AAA	GCA	GTA	GAA	ACT	CTA	AAA	AAT	AGC	ATT	AAG	CTT
	CTG	TTA	CGA A	161	J.J.T.	CGT	CAT	CTT	TGA	GAT	TTT	TTA	TCG	TAA	TTC	GAA
	U	44	^	. * -	Λ.	Α.	٧	£	T	<b>1.</b>	K	N	S	I	K	L>
9	530			540			5	50			560			570		
	•		•	•		•		•	•		•		•			•
	GAA	GGA	AGT	CTT	GTA	GTC	GGA	AAA	ACA	ACA	GTG	GAA	ATT	AAA	GAA	GGT
	E	G	TCA S	GAA L	V	CAG	CCT	K	TGT						CII	CCA
	. —	٠.		_	•	•	G		1	1	V	E	I	K	Ξ	G>
	58	30		5	90			600			61	.0		6	20	
	<b>.</b>	•	*		•		•		•	•		•	1.		• .	•
	TGA	CAA	ACT	CTA	AAA	AGA	GAA	ATT	GAA	AAA	GAT	GGA	AAA	GTA	AAA	GTC
	T	V	TGA T	L	K	R	E	TAA		K	D					
				_				_	-		ע	G	K	V	K	V>
										•			••	•		
		630			64	0		6	50	• •	٠	660	•	-	67	· O
	ىلىنى *	•	744	<b>.</b> .		•	•		50	•	•	660		•	67	
	TTT	TTG	AAT TTA	GAC CTG	ACT	GCA	GGT	TCT	50 + AAC	AAA	* AAA	660	GGT.	*	67	•
	AAA	TTG AAC	TTA	CTG	ACT TGA	GCA CGT	CCA	TCT AGA	50 AAC TTG	AAA TTT	AAA TTT	660 • ACA TGT	GGT CCA	AAA TTT	67 TGG ACC	GAA CTT
	AAA	TTG AAC L	N N	CTG	ACT TGA	GCA CGT A	CCA	TCT AGA	50 AAC TTG	AAA TTT	AAA TTT	660 • ACA TGT	GGT.	AAA TTT	67	GAA CTT
	AAA	TTG AAC L	N 80	CTG	ACT TGA	GCA CGT	CCA	TCT AGA	50 AAC TTG	AAA TTT K	AAA TTT	660 ACA TGT T	GGT CCA	AAA TTT	TGG ACC W	GAA CTT
	F	TTG AAC L	N 80	D	ACT TGA T	GCA CGT A	G G	TCT AGA S	50 AAC TTG N	AAA TTT K	AAA TTT K	660 ACA TGT T	GGT CCA G	AAA TIT K	67 TGG ACC W	GAA CTT E>
	F GAC	TTG AAC L	N 80 ACT	D AGC	ACT TGA T	GCA CGT A 690	G G	TCT AGA S	50 AAC TTG N 70	AAA TTT K	AAA TTT K	660 ACA TGT T	GGT CCA G	AAA TIT K	TGG ACC W	GAA CTT E>
	F GAC CTG	TTG AAC L AGT TCA	N 80 ACT TGA	D AGC	ACT TGA T ACT TGA	GCA CGT A 690 TTA AAT	G G ACA	TCT AGA S * ATT	50 AAC TTG N 70 AGT	AAA TTT K	AAA TTT K GAC	660 ACA TGT T	GGT CCA G 10	AAA TIT K	TGG ACC W	GAA CTT E> 720
•	F GAC CTG	TTG AAC L AGT TCA	N 80 ACT TGA	AGC TCG S	ACT TGA T ACT TGA	GCA CGT A 690 TTA AAT L	GCA G ACA TGT T	TCT AGA S * ATT	AAC TTG N 70 AGT TCA	AAA TTT K 0 * GCT CGA A	AAA TTT K GAC	660 ACA TGT T	GGT CCA G 10	AAA TIT K	TGG ACC W	GAA CTT E> 720
•	F GAC CTG	TTG AAC L AGT TCA	N 80 ACT TGA	AGC TCG S	ACT TGA T ACT TGA	GCA CGT A 690 TTA AAT L	CCA G ACA TGT T	TCT AGA S * ATT TAA I	AAC TTG N 70 AGT TCA S	AAA TTT K 0 • GCT CGA A	AAA TTT K GAC	ACA TGT T 7 AGC TCG S	GGT CCA G 10	AAA TIT K AAA TIT K	TGG ACC W	GAA CTT E> 720
	F GAC CTG D	TTG AAC L AGT TCA S	N SBO * ACT TGA T	AGC TCG S	ACT TGA T ACT TGA T	GCA CGT A 690 TTA AAT L	ACA TGT T	TCT AGA S ATT TAA I	AAC TTG N 70 AGT TCA S	AAA TTT K 0 * GCT CGA A	AAA TTT K GAC CTG D	ACA TGT T 7 AGC TCG S	GGT CCA G 10 AAA TTT K	AAA TIT K AAA TIT K	TGG ACC W ACT TGA	GAA CTT E> 720 AAA TTT K>
	GAC CTG D	TTG AAC L AGT TCA S	N 80 ACT TGA	AGC TCG S	ACT TGA T ACT TGA T	GCA CGT A 690 TTA AAT L	ACA TGT T 40	TCT AGA S ATT TAA I	AAC TTG N 70 AGT TCA S	AAA TTT K 0 * GCT CGA A	AAA TTT K GAC CTG D	ACA TGT T 7 AGC TCG S	GGT CCA G 10 AAA TTT K	AAA TIT K AAA TIT K	TGG ACC W ACT TGA	GAA CTT E> 720 AAA TTT K>

Osp b/ fla (122-234) osp c

-	770			780			79	90		1	800	,		810		
	•		•	•		•		•	•		. •		•	•		•
	ACA	GCT	GGA	ACC	AGC	CTA	GAA	GGA	TCA	GCA	AGT	GAA	ATT	AAA	AAT	CTT
	TGT	CGA	CCT	TGG	TCG	GAT	CTT	CCT	AGT	CGT	TCA	CTT	TAA	TIT	TTA	GAA
	T	A	G	T	S	L	E	G	S	A	S	E	I	Y.	N	L>
	82	20		8	330			840			8.	50			B60	
		•	> <b>*</b>		•					•		•			•	
											CCC					
											GGG					
	S	E	L	K	N	. A	_ L·	K	G	. <b>H</b> ′	_P	. M	G	К	N	S>
•		870			88	30		1	390			900	٠		9:	: n
	•	•		•	٠.	*	•	•	•		•	•		•		•
	GGG	AAA	GAT	GGG	TAA	ACA	TCT	GCA	AAT	TCT	GCT	GAT	GAG	TCT	GTT	AAA
											CGA					
	G	K	D	G	N	T	S	A	N	S	A	D	E	2	Ÿ	K>
			•													
		, 5	920			930	,		94	40		-9	950			960
	•		• .		•								•			•
											ATT					
											TAA					
est.		. •	N	<u>د</u> .	1	. E	1	>	· K	v	I	1	ט	٤	N	A>
. ''			٥.	70			980			990			100	0.0		
				•	•	•	•		•	•		•		•.	•	
	GTT	TTA	CTT	GCT	GTG	AAA	GAG	GTT	GAA	GCG	TTG	CTG	TCA	TCT	ATA	GAT
	CAA	AAT	GAA	CGA	CAC	TTT	CTC	CAA	CTT	CGC	AAC	GAC	AGT	AGA	TAT	CTA
	v	L	L	Α	$\mathbf{v}$	ĸ	E	ν	E.	A	L	L	S	S	I	D>
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L	010			1020			10:	30		10	040		_ 1			
	~ .	<b>.</b>	*.	- cim							. *					
											ATA					
											TAT					
	Ξ.	_	•	^	κ.	· 🙃 -	- <del>-</del> ·			. • • •	Į.I		. <b>V</b>	N,	14	62
	10	50		1 10	070			1080			109	90		1:	100	
		•	•		•		•	•		•		•	•		•	
	TTG	GAT	ACC	GAA	TAT	AAT	CAC	TAA	GGA	TCA	TTG	TTA	GCG	GGA	CGT	TAT
											AAC					
	L	Ð	T	E	Y	N	н	N	G	S	L	L	A	G	R	Y>
	,	1110			111	20	,	1	130			1140			1 7 5	50
	•	*		•								.140		•	11.	
	GCA	ATA	TCA							TTA	GAT	GGA	TTG	<b>ሕ</b> ሕል	AAT	GAA
											CTA					
	A	I	S	T	L	I	K	Q	ĸ	L	D	G	L	ĸ	N	, E>

FIGURE 37 (3 of 5)

Osp b/ fla (122-234) osp c 1180 1190 1160 1170 • GGA TTA AAG GAA AAA ATT GAT GCG GCT AAG AAA TGT TCT GAA ACA TTT CCT AAT TTC CTT TTT TAA CTA CGC CGA TTC TTT ACA AGA CTT TGT AAA G L K E K I D A A K K C S E T F> 1220 1210 1230 ACT AAT AAA TTA AAA GAA AAA CAC ACA GAT CTT GGT AAA GAA GGT GTT TGA TTA TTT AAT TTT CTT TTT GTG TGT CTA-GAA-CCA TTT CTT CCA CAA TNKLKEKHTDLGKEGV> 50 1260 1270 1280 ACT GAT GCT GAT GCA AAA GAA GCC ATT TTA AAA ACA AAT GGT ACT AAA TGA CTA CGA CTA CGT TTT CTT CGG TAA AAT TTT TGT TTA CCA TGA TTT DADAKEAILKTNG T K> 1300 1310 1320 1330 ACT AAA GGT GCT GAA GAA CTT GGA AAA TTA TTT GAA TCA GTA GAG GTC TGA TTT CCA CGA CTT CTT GAA CCT TTT AAT AAA CTT AGT CAT CTC CAG T K G A E E L G K L F E S V E V> 1360 1370 1380 1350 TTG TCA AAA GCA GCT AAA GAG ATG CTT GCT AAT TCA GTT AAA GAG CTT AAC AGT TTT CGT CGA TTT CTC TAC GAA CGA TTA AGT CAA TTT CTC GAA L S K A A K E M L A N S V K E L> 1430 1400 1410 1420 ACA AGC CCT GTT GTG GCA GAA AGT CCA AAA AAA CCT GGT ACC ATG GCT TGT TCG GGA CAA CAC CGT CTT TCA GGT TTT TTT GGA CCA TGG TAC CGA T S P V V A E S P K K P G T M A> 1450 1460 1470 1480 CAA TAT AAC CAA ATG CAC ATG TTA TCA AAC AAA TCT GCT TCT CAA AAT GTT ATA TTG GTT TAC GTG TAC AAT AGT TTG TTT AGA CGA AGA GTT TTA Q Y N Q M H M L S N K S A S Q N> 1490 1500 1510 1520

GTA AGA ACA GCT GAA GAG CTT GGA ATG CAG CCT GCA AAA ATT AAC ACA CAT TCT TGT CGA CTT CTC GAA CCT TAC GTC GGA CGT TTT TAA TTG TGT V R T A E E L G M Q P A K I N T>

Osp b/ fla (122-234) osp c 1550 1560 1570 • CCA GCA TCA CTT TCA GGG CTT CAA GCG TCT TGG ACT TTA AGA GTT CAT GGT CGT AGT GAA AGT CCC GAA GTT CGC AGA ACC TGA AAT TCT CAA GTA PASLSGLQASWTLRVH> 1610 1620 1600 1590 GTT GGA GCA ACC CAA GAT GAA GCT ATT GCT GTA AAT ATT TAT GCA GCT CAA CCT CGT TGG GTT CTA CTT CGA TAA CGA CAT TTA TAA ATA CGT CGA V G A T Q D E A I A V N I Y A A> 1660 1670 1650 1640 AAT GTT GCA AAT CTT TTC TCT GGT GAG GGA GCT CAA ACT GCT CAG GCT TTA CAA CGT TTA GAA AAG AGA CCA CTC CCT CGA GTT TGA CGA GTC CGA NVANLFSGEGAQTAQA> 1700 1690 1710 1720 GCA CCG GTT CAA GAG GGT GTT CAA CAG GAA GGA GCT CAA CAG CCA GCA CGT GGC CAA GTT CTC CCA CAA GTT GTC CTT CCT CGA GTT GTC GGT CGT A P V Q E G V Q Q E G A Q Q P A> . 1740 1750 1760 \* \* \* \* \* CCT GCT ACA GCA CCT TCT CAA GGC GGA GTT GGT CAC C GGA CGA TGT CGT GGA AGA GTT CCG CCT CAA CCA GTG G

FIGURE 37 (5 of 5)

PATAPSQGGVGHX>

				10			20			30		*		40		
OspC-B31	ATG TAC	AAA TTT	AAG TTC	AAT TTA	ACA TGT	TTA AAT	AGT	GCG	ATA	TTA	ATG	ACT	TTA AAT	TTT AAA	TTA AAT	TTT AAA
1. OspC-P [ 1832 ]	к	•••	:	10	•••		20	•••		30			•••	40	•••	>
2. OspC-T			_	10			20			30	•••		•	40		>
3. OspC-K	4		:	10			20	• • •		30			•••	40		>
	50										·80	•		90		•
OspC-B31	ATA TAT	TCT	TGT	AAT	AAT	TCA	GGG	AAA	GAT	GGG	* AAT	ACA	TCT	GCA	AAT	TCT
												tgc				
1. OspC-P [ 1832 ]	K50	•••	• • •	•g•	••.	• • •	• • •	•••	.g.		g	t.	90	a.t	• • •	c>
2. OspC-T																0 >
3. OspC-K [ 1774 ]	450	• • •	• • •	60	•••		t	70 ggg			.cc	80 g		a.t		0 •••>
<i>,</i> •	10	0		:	110		_	120			13	30		. 1	40	
OspC-B31	GCT (	GAT	GAG	TCT	GTT	AAA	GGG	CCT	AAT	CTT	ACA	GAA	ATA	AGT	AAA	AAA TTT
1. OspC-1 [ 1832 ]	00		:	110	.cg		120	• • •		13	30	• • •		140		>
2. OspC-T [ 1786. ]		• • •	. 10	00	.ca	:	110 a			120		'.t.	13	30		>
3. OspC-K												.t.		30	• • •	>
	;	150			16	50		3	170			180	-		19	0
OspC-B31	* ATT	* ACG TGC	GAT	* TCT	AAT	GCG	GTT	TTA	CTT	GCT.	GTG	180 * AAA TTT	GAG	* GTT CAA	GAA CTT	* GCG CGC
1. OspC-P [ 1832 ]	K150			10	50			170			180			19	0	
2. OspC-T								_							_	t>
[ 1786 ] 3. OspC-K [ 1774 ]																
[ 1774 ]	•••	a	•••	• • •	•••	a	t	g	• • g	•••		•••	a	•••	•• <b>g</b>	t>
OspC-B31	* TTG		200 *	TT-CT		210	1				*			CCT		240
	AAC	GAC	AGT	AGA	TAT	CTA	CTT	TAA	CGA	CGA	TTT	CGA	TAA	CCA	TTT	TTT
1. OspC-P [ 1832 ]	• • •	g.t	.t.	• • •	• • •	•••	• • •	c	20	aag	2	30		•••		>
2. OspC-T [ 1786 ]								210				22	20			230

Figure 38 (1 of 3)

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										-						
3. OspC-1	K4 19	0			200			210			2	20			230	
[ 1774 ]	• • •	a.c	• • •	• • •	• • •	• • •	• • •	c	• • •	aa.	• • •	• • •	• • •	• • •	• • •	gt.>
		•														
			2.	50	*	:	260			270			2	80		
•		*		*	*		*	•	*	*		*		*	*	
OspC-B31	ATA	CAC	CAA	AAT	AAT	GGT	TTG	GAT	ACC	GAA	TAT	AAT	CAC	AAT	GGA	TCA
•	TAT															
1. OspC-1 [ 1832 ]	OK.	25	-0			260 -			270		•	. ,	<b>2</b> 0			200
r 1832 i		a	a.t		•	200	а		a.t	tt.	a.,		G		'	290
		5		• • •	• • •		•••		9						•••	· · · · ·
						tac										
2 00 1						i.				000						
2. Ospc-1 [ 1786 ]	rk.		_	240	~	12:	ວບ		_	260	~~~		270	_	_	
3. OspC-1 [ 1774 ]	(4	240			2	50		:	260			270			2	80
[ 1774 ]	• • •	t		• • •		• • •	a	a	g.t	a.t	gcg	gg.	a			>
									_							
	290			300			3	10		,	330			220		
	290 *		*	300		*	٥.	*	*		32U *		*	. 330		*
OspC-B31	TTG '	TTA	GCG	GGA	CGT	TAT	GCA	ATA	TCA	ACC	CTA	ATA	AAA	CAA	AAA	TTA
	AAC	AAT	CGC	CCT	GCA	ATA	CGT	TAT	AGT	TGG	GAT	TAT	TTT	GTT	TTT	AAT
1. OspC-F [ 1832 ]	·		300		GCC.	٠	LU		•	320			330	~		
[ 2002 ]	•••	• • •	•••	• • •	gcc	• • •	• • •	• • •	• • •	• • •	• • •	•••		9	• • •	••9>
2. OspC-2	80		. 2	290			300			. 3:	10		:	320		
2. OspC-2 [ 1786 ]	• • • •	a	a	• • •	gc.	•••	.a.			.aa			.c.			>
3 0000-2	· A	_				200			_							
3. OspC-X			.90		~~~	300			٤.	10		-	320	_		330
	• • • •	• • •	•••	• • •	gcc	• • •	• • •	• • •	• • •	• • •	• • •	• • •		g	• • •	• • • >
	340	0		:	350		_	360		4.	37	70		:	380	
OspC-B31	340 GAT 0	O * GGA	* TTG	: AAA	350 *	GAA	* GGA	360 *	AAG	έ.	37	70 * **	* Cam	ece :	380	
OspC-B31	GAT C	O * GGA CCT	* TTG AAC	AAA TTT	350 * AAT TTA	GAA CTT	* GGA CCT	360 TTA AAT	AAG TTC	# GAA	37 AAA TTT	O * ATT	GAT CTA	GCG CGC	380 * GCT CGA	AAG TTC
OspC-B31	GAT (	GGA CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	ATT AAT	AAG TTC	GAA CTT	AAA TTT	ATT.	GAT CTA	GCG CGC	GCT CGA	AAG TTC
OspC-B31	GAT (	GGA CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	ATT AAT	AAG TTC	GAA CTT	AAA TTT	ATT.	GAT CTA	GCG CGC	GCT CGA	AAG TTC
OspC-B31	GAT (	GGA CCT	TTG AAC	AAA TTT	AAT	GAA CTT	GGA CCT	ATT AAT	AAG TTC	GAA CTT	AAA TTT	ATT.	GAT CTA	GCG CGC	GCT CGA	AAG TTC
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT	AAT TTA ttt	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT	AAA TTT	ATT TAA	GAT CTA 880	GCG CGC	GCT CGA	390
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT	GAT CTA 880 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT	GAT CTA 880 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT	GAT CTA 880 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT	GAT CTA 880 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ]	GAT (CTA (	GGA CCT	TTG AAC	AAA TTT 350 	AAT TTA ttt a	GAA CTT	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac.	AAA TTT G 360	ATT	GAT CTA 880 .ca	GCG CGC	GCT CGA	390 >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT (CTA (	aa. .t.	TTG AAC	AAA TTT 350 	AAT TTA ttt a 10 tca ttc	360 	GGA CCT	TTA AAT	AAG TTC	GAA CTT 70 ac. a	AAA TTT 9 360	37	GAT CTA 380 .ca a.a	GCG CGC	GCT CGA	390>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K	GAT CTA C 40 ag. a R330 ag. 4	aa. .t.	TTG AAC	AAA TTT 350	AAT TTA ttt a 10 tca ttc	360 	GGA CCT	TTA AAT	360 	GAA CTT	AAA TTT 360	37 	GAT CTA 380 .ca a.a	aa. 37.a.	GCT CGA	390>
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K	GAT CTA C 40 ag. a R330 ag. 4 ag. a	GCA CCT aa. .t.	TTG AAC	AAA TTT 350 t	AAT TTA ttt a 10 tca ttc	360  50 	GGA CCT	AAT	AAG TTC 37 360 t	GAA CTT 70 ac. a	AAA TTT 360	37 420	GAT CTA 380 .ca a.a	aa. 37.a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA C 40 ag. a R330 ag. 4	GCA CCT aa. .t.	TTG AAC	AAA TTT 350 t	AAT TTA ttt a 10 tca ttc	360  50 	GGA CCT	AAT	AAG TTC 37 360 t	GAA CTT 70 ac. a	AAA TTT 360	37 420	GAT CTA 380 .ca a.a	aa. 37.a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ]	GAT (CTA (CTA (CTA (CTA (CTA (CTA (CTA (C	aa. .t.	TTG AAC	AAA TTT 350 34 t	AAT TTA ttt a 10 ca ttc a 40 ACA TGT	GAA CTT 360  50 *TTT AAA	GGA CCT .a.	AAT TTA	AAG TTC 360 t	CAA CTT 70 ac. a	S 360 	ATT TAA 37 420 GAA CTT	GAT CTA 80 .ca a.a 0a AAA TTT	aa. 37.a. .a.	GCT CGA	390 > >
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P	GAT (CTA (ACTA (AC	aa. .t. .aa.	TTG AAC	AAA TTT 350 34 t	AAT TTA ttt a 10 tca ttc	GAA CTT 360  50 TTT AAA	GGA CCT .a. .ag ACT TGA	AAT TTA	AAA TTT	GAA CTT 70 ac. a	g 360 	ATT TAA 37	GAT CTA 380 .ca a.a 70 a	GCG CGC	GCT CGA	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ]	GAT CTA CAN ANA TTTT A	GGA CCT aa. .t.	TTG AAC	AAA TTT 350 t	AATA TTA ttt .a 10 ca ttc .a 40 ACA TGT	GAA CTT 360  50 * TTT AAA	.aag ACT TGA	AAT TTA	AAG TTC 37 360 t	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37	GAT CTA 380 .ca a.a 0 .a AAA TTT 43	aa. 37.a. CAC GTG	GCT CGA	390 > > 880 > GAT CTA
1. OspC-31  1. OspC-3 [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T	GAT CTA CAN AND TTTT F	GGA CCT aa. .t. 390* GGA	TTG AAC	AAA TTT 350 34 t GAA CTT	AATATTA tttt a 10 ca ttc a 40 ACAT ga. 390	GAA CTT 360  50 *TTT AAA	.a. .ag ACT	AAT TTA	AAG TTC 37 360 t	GAA CTT 70 ac. a TTA AAT 420 C	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 .a AAA TTT 43	aa. 37.a. CAC GTG	GCT CGA	390>> 880> GAT CTA
1. OspC-31  1. OspC-3 [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T	GAT CTA CAN AND TTTT F	GGA CCT aa. .t. 390* GGA	TTG AAC	AAA TTT 350 34 t GAA CTT	AATATTA tttt a 10 ca ttc a 40 ACAT ga. 390	GAA CTT 360  50 *TTT AAA	.a. .ag ACT	AAT TTA	AAG TTC 37 360 t	GAA CTT 70 ac. a TTA AAT 420 C	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt	GAT CTA 380 .ca a.a 70 .a AAA TTT 43	aa. 37.a. CAC GTG	GCT CGA	390>> 880> GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA CAR AND TTT A	aa. .t. aa. .gr	TTG AAC	SAA TTT 350 t	AATATTA ttta 10 ca ttca 40 ACA TGT ga. 390 .a.	GAA CTT 360 	GGA CCT .a. .ag .ag	AAT TTA	AAG TTC 35 360t 10 **AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 380 .ca a.a 0a AAA TTT 43 ggt	GCG CGC aa. 37. a. CAC GTG	GCT CGA 70  43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA CAR AND TTT A	aa. .t. aa. .gr	TTG AAC	SAA TTT 350 t	AATATTA ttta 10 ca ttca 40 ACA TGT ga. 390 .a.	GAA CTT 360 	GGA CCT .a. .ag .ag	AAT TTA	AAG TTC 35 360t 10 **AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 380 .ca a.a 0a AAA TTT 43 ggt	GCG CGC aa. 37. a. CAC GTG	GCT CGA 70  43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-31  1. OspC-3 [ 1832 ]  2. OspC-T [ 1786 ]  3. OspC-K [ 1774 ]  OspC-B31  1. OspC-P [ 1832 ]  2. OspC-T	GAT CTA CAR AND TTT A	aa. .t. aa. .gr	TTG AAC	SAA TTT 350 t	AATATTA ttta 10 ca ttca 40 ACA TGT ga. 390 .a.	GAA CTT 360 	GGA CCT .a. .ag .ag	AAT TTA	AAG TTC 35 360t 10 **AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 380 .ca a.a 0a AAA TTT 43 ggt	GCG CGC aa. 37. a. CAC GTG	GCT CGA 70  43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA CAR AND TTT A	GCA CCCT aa. .t. aa. 390*TACA	TTG AAC	SAA TTT 350 t	ATTA  OCA  CA  CA  TG  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  TG  TG  TG  TG  TG  TG  TG  TG  T	360 ************************************	a. a. ag ACT TGA	AAT TTA	AAG TTC 35 360t 10 **AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t	GAT CTA 380 .ca a.a 0a AAA TTT 43 ggt	GCG CGC aa. 37. a. CAC GTG	GCT CGA 70  43 ACA TGT 420 g	390 > > 880 > GAT CTA
1. OspC-3 [ 1832 ] 2. OspC-T [ 1786 ] 3. OspC-K [ 1774 ] OspC-B31 1. OspC-P [ 1832 ] 2. OspC-T [ 1786 ]	GAT CTA CAR AND TTT A	GCA CCCT aa. .t. aa. 390*TACA	TTG AAC	SAA TTT 350 t	ATTA  OCA  CA  CA  TG  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  3  40  ACA  TG  TG  TG  TG  TG  TG  TG  TG  TG  T	GAA CTT 360 	a. a. ag ACT TGA	AAT TTA	AAG TTC 35 360t 10 **AAA TTT	GAA CTT 70 ac. a TTA AAT 420 c	AAA TTT 360 	ATT TAA 37 37 420 GAA CTT agt 10t .gt	GAT CTA 380 .ca a.a 0a AAA TTT 43 ggt	GCG CGC aa. 37. a. CAC GTG	GCT CGA 70  43 ACA TGT 420 g	390 > > 880 > GAT CTA

Figure 38 (2 of 3)

Ospo	C-B31	CTT GAA	GGT CCA	AAA TTT	GAA CTT	GGT CCA	GTT CAA	ACT TGA	GAT CTA	GCT	GAT CTA	GCA CGT	AAA	GAA CTT	GCC	ATT TAA	TTA AAI	k C
1.	OspC-P																	
	OspC-T '86 ]																	
3. [ 17	OspC-4	30	a	gtt	440 .ct	.c.	.c.	450		.a.	. 4 c	60	•••	• • •	470 t	•••	• • •	>
											•		*					
OspC	-B31	AAA TTT	ACA TGT	AAT	GGT	ACT	AAA	ACT	AAA	GGT	GCT	GAA	GAA	עייים יי	CCA	222	ጥጥል	
[ 18	OspC-P) 32 }	K 49	90	c	.ca	500	.cc	ga.	510		•••	5: a	20	t	aa.	30 g.t	•••	>
2: [ 17	OspC-TI 86 ]	R	• • •	480 c	a	•••	49	90 gac	g			a		510	.a.	g.g		>
3. [ 17	ОврС-К 74 ]	4480 ••g	t	•••	49 cc.	0	•••	ga.	500 ••g	•••	• • •	510 a	.c.	•••	52 aa.	9.c	:	>
		530	CAA	*	540		*	5	50 *	*	5	60			570			
	201	AAA	CTT	AGT	CAT	CTC	CAG	AAC	AGT	TTT	CGT	CGA	AAA	GAG CTC	ATG TAC	CTT GAA	GCT CGA	
[ 18:	OspC-PI 32 }	•••	540	• • •	•••	55 a	o .gt		.t.	60	•••	• • •	570 C	.ta	gca	58 a	0 a	>
[ 17	OspC-52 86 ] .	2D	a	5	30	a	ag.	540	• • •	•••	55	g	c.,.	.ca	60 gca	t.a	a:	>
3. [ 17:	Оврс-К4 74 }	.c.	30	•••	• • •	540 a	ag.	•••	55 g.,	0	•••	g	60	a	gca	570 t.a	>	>
	<b>.</b>																	
	-83I	AAT TTA	TCA AGT	GTT CAA	AAA TTT	GAG CTC	CTT GAA	ACA TGT	AGC TCG	CCT GGA	GTT CAA	GTG CAC	GCA CGT	GAA CTT	AGT TCA	CCA :	TTT	
1.	OspC-PK 32 ]	•••	5	90		a	600	•••	t	61	0	a	6	20	• • •		630	•
	OspC-TR 36 ]																	
	OspC-K4		58		• • •	•	90	• • •		600	• • •	•••	61				20	•
			630						٠									
OspC-	-B31	* AAA TTT	CCT GGA	TAA ATT			:					•						
1.	OspC-PK 32 ]		•••,	•••>									-					
2. [ 178	OspC-TR 6 )	6	20	>				•										
3. [ 177	ОврС-K4 '4 ]		• • •	630 •••>														

Figure 38 (3 of 3)

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	1 B-Con	_			10			20			30				40 ·		
	1. P-Gau 2804 ]	•••	• • •	• • •	•••	•••	• • •						• • •-			• • •	>
Į	2. DK29 o 2786 ]	s ••••	•••	c	10	•••	•, • •	20	•••		30	•••	• • •	g	40	• • •	>
	3. K48 os	p			10			20			30				40		
I	2786 ]	- • • •	•••	•••	• • •	• • •	• • •	•••	•••	•••	•••	• • •	•••.	• • •	•••	•••	>
		50 *		*	60 *		*	•	70 *	*		80		•	90		
B	O ospD	AAT	GAA CTT	GGT	GTA	AAC TTG	TCA	AAA	GAT	TAC	GAG	TCA	AAA	AAA	CAG	AGT TCA	ATA TAT
	1. P-Gau	o50			60			•	70			80			90		
[	2804 }	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	•••	• • •	• • •	• • •	>
	2. DK29 o	<b>s</b> 50		-	60		•	•	70			80					
I	2786 ]	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	>
_	3. K48 os; 2786 ]	p50			60			. 7	70			80			90		
I	2786 ]	• • •	• • •	• • •	• • •	·g.	• • •	• • •	• • •	• • •	•••	• • •	• • •	•••	• • •	• • •	• • • •
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B	ospD .	CTA GAT	GGT	GAA	TTA	AAT	CAG	CTA	TTG	GGG	CAA	ACT	ACA	AAT	TCA	CTA	AAA TTT
	1. P-Gau o	<b>1</b> 0	00	-	1	10			120			13	0		1	.40	
ſ	2804 ∞].	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	>
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I	3. K48 osp 2786 ]	• • • •	•••	•••	•••	•••	• • •	• • •	120	• • •	• • •		0	• • •	1	40	>
-			150			16	o <sup>.</sup>		1	.70	·	-	180	•. <del>-</del> •		 19	O
BC	ospD	*	GCA	444	★ ••••••••••••••••••••••••••••••••••••	ארא	*	* CAT	יים מ	απυ *	ת <i>מ</i>	*	*	3 3 M	*	663	*
		CTT	CGT	TTT	TTA	TGT	TGT	CTA	TTA	AAT	TTA	CGT	AGT	TTA	CTC	CGT	TTA
r	1. P-Gau o		150							70			180			19	0
											• • •	• • •	• • •	•••	• • •	•••	>
I	2. DK29 of 2786 ]	• • •	150	• • •	• • •	16	o • • • •	• • •	1	70	•••		180	•••	• • •	19	0 • • • >
I	3. K48 osp 2786 j	•••	150		•••			•••	1	70	• • •		180	•••	· · ·	19	
				•													
		_	2	00			210			22	0	_	2	30			240
BC	ospD	AAA TTT	GTT CAA	GTA	GAA	GCA (	GTT :	ATA .	AGT	GTG	GTT	AAT '	TTA 2	TTA	TCA AGT	TCT (	* GCT CGA

-									96	/13.	3			•		
1. P-Gau [ 2804 ]	<b>o</b> .		200			210			2	20	-		230			240
[ 2804 ]	• • •	• • •	. • • •										•,••	• • •	• • •	>
2. DK29 o					•				2	20		•	230			240
[ 2786 ]		• • •	• • •	• • •		• • •	• • •	• • •	• • •	•••	•••	• • •	• • •	• • •	• • •	•••>
3. K48 os			200			210			2	20			230			240
, 2, 5,	• • • •				•••		• • • •	•••	•••	•••	•••	•••	•••	•••	• • •	•••
			2	50			260			270			2	80		
BO ospD	GCA	* GAT	CAG	* GTA		GGT			* CAA	* ATA	TGC	* ACG	ATT	* TAG	* CTC	AAA
	CGT	CTA	GTC	CAT	TTT	CCA	GTT	GTT	GTT	TAT	ACG	TGC	TAA	ATC	GAG	TTT
1. P-Gau	о ·		2	50		. :	260			270			2	80		
[ 2804 ]	• • •	• • •	•••	• • •	• • •	• • •	. • • •	• • •	• • •	• • •	• • •	• • •	. • • •	• • •	• • •	>
2. DK29 o			2										2	80		
[ 2786 ]				-					• • •		• • •	•••	• • •	• • •	• • •	>
3. K48 os [ 2786 ]	P		2	50		•	260			270			2	80		
		•••		•••	•••	•••	•••	•••	•••	• • •	•••		•••	• • •	• • •	•••>
	290			300			3.	10	*		320			330		
BO ospD	* TGG	CAG		★ DAT	A ጥጥ	* ™AG	מממ	*	* ««۳	AGG	* ጥልል	Cury	*	*		*
	ACC	GTC	TTT	ATC	TAA	ATC	TTT	TTT	ATT	TCC	TTA	GAT	CAC	TAT	TTC	ATT
1. P-Gau	290			300				10			320			330		
[ 2804 ]	• • •	• • •	• • •	• • •	• • •	• • •		•. • •	• • •	• • •	• • •	• • •	• • •		• • •	>
2. DK29 of	290			300			3	10		. :	320			330		
[ 2786 ]	• • •	• • •	• • •	• • •	• • •	•••	• • •	•••	• • •	• • •	• • •	• • •		• • •	• • •	>
3. K48 os:				300				10			320			330		_
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	34	10			350			360			31	70	٠	3	80	
BO ospD	TAG	* TTG	* CGG	СТА	* ATG	ጥጥር	*	*	AAG	* CDT	מידמ	*	* ⊄™™		*	C) G
	ATC	AAC	GCC	GAT	TAC	AAC	GCT	TTC	TTC	GTA	TAT	TGG	AAT	GAT	TIC	CAG GTÇ
1. P-Gau	34	10		3	350			360			37	70		3	80	
[ 2804 ]	•••	• • •	•••	• • •	. • • •	• • •	• • • .	•••	• • •	• • •	• • •	• • •	• • •	•••	•••	>
2. DK29 of	3 34	10	•	3	350			360			37	70		3	80	•
[ 2786 ]	•••	• • •	• • •	• • •	• • •	• • •	•••	• • •	• • •	• • •	• • •	• • •	• • •	•••	•••	>
3. K48 osp	34	10		3	350			360			37	70		3	80	
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BO ospD	* TAG	* AAC	מממ	* ኳጥል	TGC	*	*	TO TO	*	220	*	*		*		*
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1. P-Gau	>	390			40	00		4	110			420			43	٥
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2. DK29 os	3	390			40	0		4	110			420			43	0

Figure 39 (2 of 4)
SUBSTITUTE SHEET (RULE 26)

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		630			64	40		(	650			660		_	61	
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1. P-Gau [ 2804 ]	•	630	•••	• • •		10	• • •	• • •	650 a	•••	• • •	660	•••	•••	67	70 >
2. DK29 o [ 2786 ]	s •••									•••		660	•••		67	70 >
3. K48 os [ 2786 ]	P	630	•••	•••		10	•••		650 a	•••	•••	660	•••	•••		70
. •	.÷	. (	580 *		*	690		*	76	00			•			<u>.</u>
BO ospD										TAC ATG			,			-
1. P-Gau [ 2804 ]	•	• • •	680	•••	• • •	690	<i></i>	•••		00	>					
2. DK29 o [ 2786 ]	s •••	• • •	680	• • •	•••	690	• • •	•••	· 70	00	>					
3. K48 os [ 2786 ]					•••	690	• • •	• • •		00	>	•				

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															TTA
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50			60			7	70			80			90		
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CJA	Ile	Asn	Ala.	Ala	Asn	Leu	Ser	Lys	Thr	Gln	Glu	Lys	Leu	Ser	Ser>
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Gly	.,.	··- 9										O <sub>2</sub>		Gry	.017
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			TAA												
Ser	Gly	Lys	Ile	Asn	Ala	Gln	Ile	Arg	Gly	Leu	Ser	Gln	Ala	Ser-	Arg>
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	3	200		•	210		. •	22	20	•	2	230			240
• TAA		•	AAG	• GCT	•	ТАА	. • TTT		•	+ ACA		•	ദൈ	• AAT	•
	ACT	• TCA	AAG TTC		• ATT			ATT	• CAG		ACA	GAA			TTA
TTA	ACT TGA	TCA AGT	TTC	CGA	ATT TAA	TTA	AAA	ATT AAT	* CAG GTC	TGT	ACA TGT	GAA CTT	CCC	TTA	TTA
TTA	ACT TGA	TCA AGT	TTC	CGA	ATT TAA	TTA	AAA	ATT AAT	* CAG GTC	TGT	ACA TGT	GAA CTT	CCC	TTA	TTA AAT
TTA	ACT TGA	TCA AGT Ser	TTC	CGA	ATT TAA Ile	TTA	AAA	ATT AAT	* CAG GTC	TGT	ACA TGT	GAA CTT Glu	CCC	TTA	TTA AAT
TTA Asn	ACT TGA Thr	TCA AGT Ser	TTC Lys	CGA Ala	ATT TAA Ile	TTA Asn 260	AAA Phe	ATT TAA Ile	CAG GTC Gln 270	TGT Thr	ACA TGT Thr	GAA CTT Glu	CCC Gly	TTA Asn	TTA AAT Leu>
TTA Asn AAT	ACT TGA Thr	TCA AGT Ser 29	TTC Lys 50 GAA	CGA Ala	ATT TAA Ile	TTA Asn 260 TTA	AAA Phe GTA	ATT TAA Ile •	CAG GTC Gln 270	TGT Thr	ACA TGT Thr	GAA CTT Glu 28	CCC Gly 30 • GCA	TTA Asn	TTA AAT Leu>
TTA Asn AAT TTA	ACT TGA Thr GAA CTT	TCA AGT Ser 2! GTA CAT	TTC Lys 50 GAA CTT	CGA Ala AAA TTT	ATT TAA Ile GTC CAG	TTA Asn 260 TTA AAT	AAA Phe GTA CAT	ATT TAA Ile AGA TCT	CAG GTC Gln 270 ATG TAC	TGT Thr AAG TTC	ACA TGT Thr GAA CTT	GAA CTT Glu 28 TTG AAC	CCC Gly 30 • GCA CGT	TTA Asn GTT CAA	TTA AAT Leu> CAA GTT
TTA Asn AAT TTA	ACT TGA Thr GAA CTT	TCA AGT Ser 2! GTA CAT	TTC Lys 50 GAA CTT	CGA Ala AAA TTT	ATT TAA Ile GTC CAG	TTA Asn 260 TTA AAT	AAA Phe GTA CAT	ATT TAA Ile AGA TCT	CAG GTC Gln 270 ATG TAC	TGT Thr AAG TTC	ACA TGT Thr GAA CTT	GAA CTT Glu 28 TTG AAC	CCC Gly 30 • GCA CGT	TTA Asn GTT CAA	TTA AAT Leu>
AAT TTA ASN	ACT TGA Thr GAA CTT	TCA AGT Ser 2! GTA CAT	TTC Lys 50 GAA CTT Glu	CGA Ala AAA TTT	ATT TAA Ile GTC CAG	TTA ASD 260 TTA AAT Leu	AAA Phe GTA CAT Val	ATT TAA Ile AGA TCT	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC	ACA TGT Thr GAA CTT	GAA CTT Glu 28 TTG AAC	CCC Gly 30 • GCA CGT Ala	TTA Asn GTT CAA	TTA AAT Leu> CAA GTT
TTA Asn AAT TTA	ACT TGA Thr GAA CTT	TCA AGT Ser 2! GTA CAT	TTC Lys 50 GAA CTT	CGA Ala AAA TTT	ATT TAA Ile GTC CAG	TTA ASD 260 TTA AAT Leu	AAA Phe GTA CAT	ATT TAA Ile AGA TCT	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC Lys	ACA TGT Thr GAA CTT	GAA CTT Glu 28 TTG AAC	CCC Gly 30 • GCA CGT	TTA Asn GTT CAA	TTA AAT Leu> CAA GTT
AAT TTA Asn	ACT TGA Thr GAA CTT Glu	TCA AGT Ser 25 GTA CAT Val	TTC Lys 50 GAA CTT Glu	CGA Ala AAA TTT Lys	ATT TAA Ile GTC CAG Val	TTA Asn 260 TTA AAT Leu	AAA Phe GTA CAT Val	ATT TAA Ile AGA TCT Arg	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC Lys	ACA TGT Thr • GAA CTT Glu	GAA CTT Glu 28 TTG AAC Leu	CCC Gly 30 GCA CGT Ala 330	TTA Asn GTT CAA Val	TTA AAT Leu> CAA GTT Gln>
AAT TTA Asn 290 TCA	ACT TGA Thr GAA CTT Glu	TCA AGT Ser 25 GTA CAT Val	TTC Lys 50 GAA CTT Glu 300	CGA Ala AAA TTT Lys	ATT TAA Ile GTC CAG Val	TTA Asn 260 TTA AAT Leu 31	AAA Phe GTA CAT Val	ATT TAA Ile * AGA TCT Arg	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC Lys 320	ACA TGT Thr GAA CTT Glu	GAA CTT Glu 28 TTG AAC Leu	CCC Gly 30 GCA CGT Ala 330	TTA Asn GTT CAA Val	TTA AAT Leu> CAA GTT Gln>
AAT TTA Asn 290 TCA AGT	ACT TGA Thr GAA CTT Glu GGT CCA	TCA AGT Ser 25 GTA CAT Val AAC TTG	TTC Lys 50 GAA CTT Glu 300 GGC CCG	CGA Ala AAA TTT Lys ACA TGT	ATT TAA Ile GTC CAG Val TAT ATA	TTA ASD 260 TTA AAT Leu 31 TCA AGT	AAA Phe GTA CAT Val 10 * GAT CTA	ATT TAA Ile * AGA TCT Arg GCA CGT	CAG GTC Gln 270 ATG TAC Met	AAG TTC Lys 320 AGA TCT	ACA TGT Thr GAA CTT Glu GGT CCA	GAA CTT Glu 28 TTG AAC Leu TCT	CCC Gly 30 GCA CGT Ala 330 ATA TAT	TTA Asn GTT CAA Val CAA GTT	TTA AAT Leu> CAA GTT Gln> ATT
AAT TTA ASN  290 TCA AGT Ser	ACT TGA Thr GAA CTT Glu GGT CCA Gly	TCA AGT Ser 25 GTA CAT Val AAC TTG	TTC Lys 50 GAA CTT Glu 300 GGC CCG Gly	CGA Ala AAA TTT Lys ACA TGT Thr	ATT TAA Ile GTC CAG Val TAT ATA	TTA ASD 260 TTA AAT Leu 31 TCA AGT	AAA Phe GTA CAT Val 10 * GAT CTA Asp	ATT TAA Ile * AGA TCT Arg GCA CGT	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC Lys 320 AGA TCT Arg	ACA TGT Thr GAA CTT Glu GGT CCA Gly	GAA CTT Glu 28 TTG AAC Leu TCT	CCC Gly 30 GCA CGT Ala 330 ATA TAT Ile	TTA ASD GTT CAA Val CAA GTT Gln	TTA AAT Leu> CAA GTT Gln> ATT TAA
AAT TTA ASN  290 TCA AGT Ser	ACT TGA Thr GAA CTT Glu GGT CCA	TCA AGT Ser 25 GTA CAT Val AAC TTG	TTC Lys 50 GAA CTT Glu 300 GGC CCG Gly	CGA Ala AAA TTT Lys ACA TGT	ATT TAA Ile GTC CAG Val TAT ATA	TTA ASD 260 TTA AAT Leu 31 TCA AGT	AAA Phe GTA CAT Val 10 * GAT CTA	ATT TAA Ile * AGA TCT Arg GCA CGT	CAG GTC Gln 270 ATG TAC Met	TGT Thr AAG TTC Lys 320 AGA TCT Arg	ACA TGT Thr GAA CTT Glu GGT CCA	GAA CTT Glu 28 TTG AAC Leu TCT	CCC Gly 30 GCA CGT Ala 330 ATA TAT Ile	TTA Asn GTT CAA Val CAA GTT	TTA AAT Leu> CAA GTT Gln> ATT TAA
AAT TTA ASN 290 TCA AGT Ser	ACT TGA Thr GAA CTT Glu GGT CCA Gly	TCA AGT Ser 2: GTA CAT Val AAC TTG ASD	TTC Lys 50 GAA CTT Glu 300 GGC CCG Gly	AAA TTT Lys ACA TGT Thr	ATT TAA Ile GTC CAG Val TAT ATA TYr	TTA ASD 260 TTA AAT Leu 31 TCA AGT Ser	GTA CAT Val GAT CTA Asp 360	ATT TAA Ile * AGA TCT Arg GCA CGT Ala	CAG GTC Gln 270 ATG TAC Met GAC CTG Asp	TGT Thr AAG TTC Lys 320 AGA TCT Arg	ACA TGT Thr GAA CTT Glu GGT CCA Gly	GAA CTT Glu 28 TTG AAC Leu TCT AGA Ser	CCC Gly 30 GCA CGT Ala 330 ATA TAT Ile	TTA ASD  GTT CAA Val  CAA GTT GlD	TTA AAT Leu> CAA GTT Gln> ATT TAA Ile>
AAT TTA ASN 290 • TCA AGT Ser 3	ACT TGA Thr GAA CTT Glu GGT CCA Gly	TCA AGT Ser 2: GTA CAT Val AAC TTG ASD	TTC Lys 50 GAA CTT Glu 300 GGC CCG Gly	CGA Ala AAA TTT Lys ACA TGT Thr	ATT TAA Ile GTC CAG Val TAT ATA TYT	TTA ASD 260 TTA AAT Leu 31 TCA AGT Ser GAC	AAA Phe GTA CAT Val  GAT CTA Asp 360 GAA	ATT TAA Ile AGA TCT Arg GCA CGT Ala	CAG GTC Gln 270 ATG TAC Met GAC CTG ASP	TGT Thr AAG TTC Lys 320 AGA TCT Arg	ACA TGT Thr GAA CTT Glu GGT CCA Gly	GAA CTT Glu 28 TTG AAC Leu TCT AGA Ser	CCC Gly 30 GCA CGT Ala 330 ATA TAT Ile	TTA ASD  GTT CAA Val  CAA GTT GlD  B80 CAA	TTA AAT Leu>  CAA GTT Gln> ATT TAA Ile>
AAT TTA ASN CTT Ser	ACT TGA Thr GAA CTT Glu GGT CCA Gly 40	TCA AGT Ser 2: GTA CAT Val AAC TTG ASD CTC	TTC Lys 50 GAA CTT Glu 300 GGC CCG Gly CAA GTT	CGA Ala AAA TTT Lys ACA TGT Thr 350 CTT GAA	ATT TAA Ile GTC CAG Val TAT ATA TYr ACA TGT	TTA ASD 260 TTA AAT Leu 31 TCA AGT Ser GAC CTG	AAA Phe GTA CAT Val  GAT CTA ASP 360 GAA CTT	ATT TAA Ile AGA TCT Arg GCA CGT Ala	CAG GTC Gln 270 ATG TAC Met GAC CTG ASP	TGT Thr AAG TTC Lys 320 AGA TCT AGA TCT	ACA TGT Thr GAA CTT Glu GGT CCA Gly 70 ATT TAA	GAA CTT Glu 28 TTG AAC Leu TCT AGA Ser	CCC Gly 30 GCA CGT Ala 330 ATA TAT Ile	TTA ASD  GTT CAA Val  CAA GTT Gln  80 . CAA GTT	TTA AAT Leu> CAA GTT Gln> ATT TAA Ile>

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FIGURE 40 (3 of 3)

Search Analysis for Sequence: B31-41kD Matrix: DNA database matrix

# 102/133

#### Alignment List

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B31-41kD	CCC	ATT AAT	AAC	GCT CGA	GCT CGA	AAT TTA	CTT	AGT TCA	AAA	ACT TGA	CAA GTT	GAA CTT	AAG TTC	CTT GAA	TCT AGA	AGT TCA
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1	3672 ]	• • •	•••	• • •	•••	•••	a	tc.	• • •	t	• • • •	•••	····	• • •	•••	• • •	>
		530 *		*	540	•	•	5	50	*		560		•	570	ı	_
B		GTT CAA	GGA	GCA	ACC	CAA GTT	GAT CTA	GAA CTT	GCT CGA	TTA AAT	GCT CGA	GTA CAT	AAT ATT	TTA A	TAT	GCA CGI	GCT
I	1. KA-41k 3996 ]	530	•••	•••	540 .a.	•••	•••		50	• • •	•••	560	•••	• • •	570		>
	2. P-Gau-	530			540			5	50			EEN					
Ĺ	2030	••9	• • •	. • • •	.at	• • •	• • •	• • •	a	• • •	•••	• • •	• • •	•••	• • •	t	>
ſ	3. BO-41k 3684 ]	530 g	• • •		540 .at	•••	•••	5!	50 a	• • •	•••	560		•••	570	t	>
Į	4. DK29-4 3672 ]	530 g	•••		540 .at		•	55	50 g	• • •		560	• • •	• • •	570	. +	
	5. PKO-41 3672 ]	530			540			. = 0	- ^								
•	,	9	•••	•••		•••	•••	•••	a	• • •	•••	•••	•••	• • ,•	•••	t	•••>
			B0 *	*	!	590		*	600		*	61	.0	•	.6	520	
B3	31-41kD	AAT TTA	GTT CAA	GCA CGT	AAT TTA	CTT GAA	كلمك	ىلىكى	CCT	CAC	CCA	~~	~		GCT CGA	_	GCT CGA
r	1. KA-41ki	5 5	30			500			600			٠.	_				
	3996 ]												•••.	• • •	• • •	• • •	>
I	2. P-Gau-6 3696 ]	• • • •	•••			590	t	g	600	• • •		61	.0	α	6	20	
	3. BO-41ki																• • • •
I	3684 ]	• • •	• • •	•••	•••	•••	t	g	•••	• • •	• • •	•••	• • •	g.,	•••		>
ſ	4. DK29-43 3672 ]	L 58	30		5	590			600			61	.0		6	20	
				•••				• • •	• • •	a	•••	. • • •	g	g	• •	• • •	a>
	5. PKO-41) 3672 ]			•••		90		g.,	600		•	61	0	<b>a</b>	6	20	>
I	20.2 ]							_				•••	• • •	9	• • •		>
1	20.2																
ł		*	630				10		€	50			660			67	0
		* GCA	630 * CCG	GTT	* CAA	64 GAG	GGT	* GTT CAA	CAA	CAG	CAA	CCA	~	~ ~ ~		67	*

1. KA-41kD [ 3996 ]	630	640	650	660	670
2. P-Gau-4 [ 3696 ]	630 t	640	650 g.a	660 g .	670 .a a>
3. BO-41kD [ 3684 ]	630 t	640	650	660	
4. DK29-41		640	650	660	
5. PKO-41k	630 t	640	CEA		
721 411p	680	690 *		710	720
, , , , , , , , , , , , , , , , , , , ,	CGA TOT COT GG	n nun uil	CCG CCT CAA	AAT TCT CCT GT ITA AGA GGA CA	
1. KA-41kD [ 3996 ]	680	690	700	710	720
2. P-Gau-4 [ 3696 ]		690 . a	700	710	720
3. BO-41kD [ 3684 ]		690	700	71.0	720
4. DK29-41 [ 3672 ]	680g	690 g	700	710	
5. PKO-41k [ 3672 ]	680	600	200		
•	730	740	750	760	
B31-41kD ACA TGT	ACT ACA GIT GAT TGA TGT CAA CTA	GCT AAT A	ACA TCA CTT G TGT AGT GAA C	CT AAA ATT GAA GA TTT TAA CTT	AAT GCT TTA CGA
1. KA-41kD [ 3996 ]	730	740		760	>
2. P-Gau-4 [ 3696 ]	730 c	740	750	760	
3. BO-41kD [ 3684 ]	730 c	740	. 750	760	
4. DK29-41 [ 3672 ]	730 c	740	750		>
5. PKO-41k	730 c	740	750		>
					- · · · · · · ·

	770		780		790	0	•	. 8	00		•	810		
B31-41kD	ATT AG	ATG		GAT	CAA A	AGG (	GCA	TAA	TTA	GGT	GCT	TTC	CAA	AAT ATT
1. KA-411 [ 3996 ]			780	• • •	790	0	• • •					810	• • •	>
2. P-Gau [ 3696 ]	-770 		780		79: • • •	0 a	•••		300	•••	• • •	810	• • •	·>
3. B0-41 [ 3684 ]	k770	• • • •	780	• • •	79: • • •	0 a			300		•••	810	• • •	>
4. DK29-	4770 		780 		79	0 a			300 -	•	•	810	• • •	>
5. PKO-4 [ 3672 ]	1770		780 ::····								•••	810	.•••	>
	820		830	•		840		•	85	50	*	8	360	
B31-41kD	AGA CT	T GAA		AAG	TAA.	AGT	ACT	GAG	TAT	GCA	ATT TAA	GAA CTT	AAT TTA	CTA GAT
1. KA-41 [ 3996 ]	kD 820													>
2. P-Gau [ 3696 ]														>
3. BO-41 [ 3684 ]														>
4. DK29- [ 3672 ]					g							-	360 c	>
5. PKO-4 [ 3672 ]	1k 820	• • • •	830	• • •	•••	840 c	•••	•••		50 t	•••		360	>
•	87	'0 *	<b>*</b>	80	*	8	89 <b>0</b>		•	900	,	•	91	.0
B31-41kD	AAA GO	A TCT	TAT GCT	CAA GTI	ATA TAT	AAA TTT	GAT CTA	GCT CGA	ACA TGT	ATG	ACA	GAT	GAG	GIT
	lkd 87		3						•••			•••	91	
2. P-Gav [ 3696 ]	u-4 8°													10
3. BO-4:	8.												9:	10
4. DK29	-41 8									900				10

5: PKO-41 [ 3672 ]	k 		•••••		•••		890	• • •	•••	900	• • •	• • •	9	10
	•	920		930			9	40		9	950			960
B31-41kD	GTA. (	GCA GCA CGT CGT	ACA AC	ייניממידי	יאדי ע	ستمليان	W 1	101					*	*
1. KA-41kI [ 3996 ]		920	**	030			•	4.0						
2. P-Gau-4	1	920		030			_	/				•		
3. BO-41kr [ 3684 ]		920	•••	930			9/							
4. DK29-41 [ 3672 ]		920		030				_						
5. PKO-41k [ 3672 ]	••••	920 t		930 a	.gt	•••	94	0 t	• • •	9	50	•••	•••	960
`				91			*				100		•••	•••>
B31-41kD	ATT G TAA C	CG CAG	GCT AAT CGA TTA	CAA (	TTE	~~~	~			* MTG :		*	TTC	AGA
1. KA-41kD		97		98	30			990			100	0		
2. P-Gau-4 [ 3696 ]		97 .a	0	98	30	t							•••	••••
3. BO-41kD [ 3684 ]		97	n	0.0			_					)	• • • •	
4. DK29-41 [ 3672 ]	•	97	^					٠.					• • •	
5. PKO-41k [ 3672 ]		971		98		t .		90				)	• • • •	•••
101	0										•		•	•••
	AA TT		•											
2. P-Gaul01 [ 3696 ] .	0 >													

Sequence Ran	ge: 1 1	:0 822				•								
		10	· ·	_	20			30		*	40		*	
OspA-B31	ATG AA TAC TT	AAA A TTT 1	TT TAT ATA ATA	A TTG T AAC	GGA CCT	ATA TAT	GGT CCA	CTA	ATA TAT	TTA AAT	GCC T CGG.A	TA . AT .	ATA TAT	CCT CCT
OspA-B31 [ 3288 ]					20	•••		30		•••	40	••	•••	>
Ospa-Ka [ 3288 ]	:•				20	•••	• • •	30	• • •	•••	40	• •	• • •	•••>,
Ospa-N40 [ 3276 ]	•••		o 		20	•••		30		•••	40	••	• • •	>
OspA-ZS7 [ 3264 ]			o 	· • • •	20			30			40	- •	• • •	>
OspA-25015 [ 2802 ]		1	0		20	. • • •		30	• • •		40 t.	• •		>
OSPA-TRO [ 2648 ]		1	0		20		• • •				40	••		>
OspA-K48 [ 2584 ]			0		20		• • •	30 			40	• •		>
Ospa-HE 11 [ 2580 ]			0		20 	•••	•••	30	• • •		40	• •	• • •	>
Ospa-DK29 [ 2566 ]			0		20			30			40	• •		>
OspA-Ip90 [ 2562 ]					20			30			40 a .			>
OspA-B0 [ 2558 ]			.0,		20			30		• • • .	40	) · • •.	• • •	>
OSPA-IP3 [ 2558 ]			.0		20		•••	30	•••		40			>
OspA-PKO [ 2558 ]			io		20			30	• • •	•••	40	•••	• • •	>
Ospa-acai [ 2556 ]	• • • •	: 			20			30	• • •	•••	40		· · ·	>
ospA-P-GAU [ 2544 ]			10	••••	20	• •••	•	30	•••	•••	4(	•••	•••	>
	50 *	*	60	*	•	70		•	80		•	90		ŧ
OspA-B31	TGT A ACA T	AG CAA TC GTT	AAT C	DA TE	C AG	CTT G GA	CIY	GAG CTC	AAA TTT	AAC	AGC TCG	GTT CAA	TCA AGT	CAT

FIGURE 42 (1 of 16)

	/	
111	<i>//3</i> 3	

OspA-B31 [ 3288 ]	50	60 	70	80	90
Ospa-Ka [ 3288 ]	50:	60	70	80	90
Ospa-N40 [ 3276 ]	50	60	70	80	90
OspA-ZS7 [ 3264 ]	50	60	70	80	90
OspA-25015 [ 2802 ]	50	60	70	80	90
OspA-TRO [ 2648 ]	50	60	70 t	80	90
OspA-K48 [ 2584 ]	50	60	70	80at	90
OspA-HE 11 [ 2580 ]	50	60	70 t	80 at	90
Ospa-DK29 [ 2566 ]	50	60	70 t	80 at	90
OspA-Ip90 [ 2562 ]	50	60	70	80 at	90
0spA-B0 [ 2558 ]	50	60	70	80 a	90 .c>
OSPA-IP3 [ 2558 ]	50c	60	70 t	80 a	90 .c>
Ospa-PKO [ 2558 ]	50 c	60	70 t	80 a	90 .c>
Ospa-ACAI [ 2556 ]	50	60	70 t	80 a	90 .c>
ospA-P-GAU [ 2544 ]	50	60	70 t	80 a	90 .c>
	100	110	120	130	140
OspA-B31	GAT TTG CCT CTA AAC GGA	GGT GAA ATY	G AAA GTT CTT C TTT CAA GAA	GTA AGC AAA GAA CAT TCG TTT CTT	AAA AAC AAA TTT TTG TTT
OspA-B31 [ 3288 ]	100	110	120	130	140>
Ospa-Ka [ 3288 ]	100	110	120	130	140>
0spA-N40	100	110	120	130	140

FIGURE 42 (2 of 16)

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		*		
[ 3276 ]		c		
OspA-ZS7 [ 3264 ]	100	110 c	120 130	>
OspA-25015 [ 2802 ]	100	110	120 130	
OspA-TRO [ 2648 ]	100	110	120 130	140 g>
OspA-K48 [ 2584 ]	100	110 gc.	120 130 t	140 g>
OspA-HE 11 [ 2580 ]	100	110 g	120 -130 t	140 g>
OspA-DK29 [ 2566 ]	100	110 gc.	120 130 t	140 g>
OspA-Ip90 [ 2562 ]	100	110 g c	120 130 t	140 g>
OspA-BO [ 2558 ]		= :	120 130 t	140 g>
OSPA-IP3 [ 2558 ]	100		120 130	140 g>
OspA-PKO [ 2558 ]	100	110 ·	120 130 t	140 g>
OspA-ACAI [ 2556 ]	100		120 ' 130 t	140 g>
ospa-P-GAU [ 2544 ]	. 100		120 130 t	140 g>
	150	160	170 180	190
OspA-B31	GAC GGC AAG T	AC GAT CTA ATT	GCA ACA GTA GAC AAG CGT TGT CAT CTG TTC	CTT GAG CTT AAA GAA CTC GAA TTT
OspA-B31 [ 3288 ]	150	160	170 180	190
Ospa-Ka [ 3288 ]	150	160	170 180	190
OspA-N40 [ 3276 ]	150	160	170 180	190>
OspA-ZS7 [ 3264 ]	150	160	170 180	190
OspA-25015 [ 2802 ]	150	160	170 180	190

FIGURE 42 (3 of 16)

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OspA-TRO [ 2648 ]	t	150 :t		a	. ag	160		g	170	• • •		18	0	a	• • •	190
OspA-K48 [ 2584 ]	• • •	150		a		160		g	170		• ••	18	0			190
OspA-HE 11 [ 2580 ]		150		a			• • • • •					18 a	_		: • • •	190
OspA-DK29 [ 2566 ]		150 t					. ga					18	0			190
OspA-Ip90 [ 2562 ]	t	150 t		٠			9				• • • •	18		• ••		190
OspA-BO [ 2558 ]	•••	150 t		• • •		160			170	•••	• ••	180	o . a	• • • •		190 a>
OSPA-IP3 [ 2558 ]	•••	150 t				160		٠.,	170	• • •	• • • •	180	) .			190 a>
Ospa-PKO - [ 2558 ]	•••	150 t	•••	•••		.60			170	•••	•••	180	a	•••	:	190
Ospa-acai [ 2556 ]	• • •	150 t	•••			.60	.ag	• • • •	170	•••	•••	180	a	•••	1 a	.90
ospA-P-GAU [ 2544 ]	•••	150 t	•••	•••	ag.	60	.ag	• • •	170	• • •	•••	180	a	•••	1 a	90.
	*	2	200			210			2:	20	•	:	230			240
OspA-B31	GGA CCT	ACT TGA	TCT AGA	GAT CTA	AAA TTT	AAC	AAT TTA	GGA CCT	TCT AGA	GGA CCT	GTA CAT	CTT GAA	GAA CTT	GGC CCG	GTA CAT	AAA TTT
OspA-B31 [ 3288 ]	•••	2	00	•••	• • •	210	•••				•••	·	230	• • •		240
Ospa-Ka [ 3288 ]	•••	2	00	•••		210	•••			0	•••	····2			•••	240
Ospa-N40 [ 3276 ]	·	2	00	•••	• • •	210	•••			0	•••		230	•••		240
Ospa-zs7 [ 3264 ]	•••	2	00	•••	•••	210	•••				•••		30	•••	•••	240
OspA-25015 [ 2802 ]	•••	a	00	• • •	•••	210	•••	• • •		0 g	• • g	2	30	• • •		240
OspA-TRO [ 2648 ]	•••		00	• • •	•••	210 .g.	c	t			ac.	2	30	t	.a.	240
OspA-K48 [ 2584 ]			00			210	c	t	22		ac.	2	30		_	240

FIGURE 42 (4 of 16)

a	200 210	220	230 240
OSDA-HE 11 [ 2580 ]		t ac.	t .a>
OspA-DK29 [ 2566 ]	200 210	220 t ac.	230 240>
OspA-Ip90 [ 2562 ]	200 210c	220 t ac.	230 240>
OspA-B0 [ 2558 ]	200 210 g	220 tgg	230 240 ac>
OSPA-IP3 [ 2558 ]	200 210 g	220 tg	230 240>
OSPA-PKO [ 2558 ]	200 210	220 tgg	230 240>
Ospa-ACAI [ 2556 ]	200 210	220 tg	230 240>
ospa-P-GAU [ 2544 ]	200 210	220 tg	230 240>
	250 260	270	280
OspA-B31	GCT GAC AAA AGT AAA GTA AAA TI CGA CTG TIT TCA TIT CAT TIT AA	A ACA ATT TCT	# # # # # GAC GAT CTA GGT CAA
OspA-B31 [ 3288 ]	250 260	270	280>
OspA-KA [ 3288 ]	250 260	270	280>
OspA-N40 [ 3276 ]	250 260	270	280>
OspA-ZS7 [ 3264 ]	250 260	270	280>
OspA-25015 [ 2802 ]	250 260	270 g	280 a.c ac.>
Ospa-TRO [ 2648 ]	250 260 tc	270	280 a a a>
OspA-K48 [ 2584 ]	250 <b>260</b>	270 g	280 tc a>
OspA-HE 11 [ 2580 ]		270 g	280 g a a>
OspA-DK29 [ 2566 ]	250 260 a	270 c g	280 tc a>
OspA-Ip90	250 260	270	280

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,,,	//75

	[ 2562 ]	a	•••	• • •	• • • •		.c.		• • •	•••	• • •	g.,	9	• • • •	• • •	a	a>
	OspA-BO [ 2558 ]	.a.	٠		250	•••		260			270 		•••		80	• • •	a>
	OSPA-IP3 [ 2558 ]	.a.			250	•••		260			270		•••		80	a.,	a>
	OspA-PKO [ 2558 ]	.a.			50	•••		260		•••	270		•••	2	80	• • •	a>
	Ospa-ACAI [ 2556 ]	.a.	•••		50		.c.	260		•••	270	g	•••		во	a	a`>
	ospa-P-GAU [ 2544 ]				50	•••		260	•••		270.		• • • •	21	BO	a	a>
		290		22	300		_		10	_	:	320		*	330		
	OspA-B31	ACC TGG	ACA TOT	CTT	GAA CTT	GTT CAA	TTC AAG	AAA	GAA	GAT	GGC	AAA TTT	ACA TGT	CTA	CTA	TCA AGT	AAA TTT
	OspA-B31 [ 3288 ]	290		• • •	300		• • •	31				20	• • •	• • •	330	• • •	>
	Ospa-Ka [ 3288 ]	290	• • •		300			31	.0		3	20			330		•
	Ospa-N40 [ 3276 ]	290	• • •		300		•••				_	20			330		>
	Ospa-ZS7 [ 3264 ]	290						.31		•••		20	• • •	· • • •	330	• • •	>
	OspA-25015 [ 2802 ]						a	31	0			20	• • •	t	330 g	• • •	>
	Ospa-TRO [ 2648 ]	290		t	300				0	• • •		20	•••	t	330	• • •	>
	OspA-K48 [ 2584 ]	290 t				a		31	0	• • •	.c.	20			330	• • •	>
	Ospa-HE 11 [ 2580 ]				300	a.c	•••	31	0	•••		20	1	t :	330	g	>
1	OspA-DK29 [ 2566 ]					a		31	0	• • • •	32	20	1	: :,	330	•••	· · ·> ִ
	OspA-Ip90 [ 2562 ]	290	• • •		300	a.c	•••	310			32		1		330		>
	OspA-BO [ 2558 ]	290	• • •	t.c	300	c	•••	310		•••		20	t	3	330 g .	`	.g.>
	OSPA-IP3 [ 2558 ]	290			300	•		310	)		32	20		-	130		

FIGURE 42 (6 of 16)

OspA-PKO [ 2558 ]	290 t.c	300	310	320 t	330 gg.>
OspA-ACAI [ 2556 ]	290	300	310		330
ospa-P-GAU [ 2544 ]	290	300	310		330
	340	350	360	· 370	380
OspA-B31	AAA GTA ACT TTT CAT TGA	TCC AAA GAC AGG TTT CTG	AAG TCA TCA TTC AGT AGT	ACA GAA GAA AAA TGT-CTT-CTT-TTT	TTC AAT GAA AAG TTA CTT
OspA-E31 [ 3288 ]	340	350	360	370	380>
Ospa-Ka [ 3288 ]	340	350		370	380
Ospa-N40 [ 3276 ]	340	350	360		380
Ospa-ZS7	340	350	360	370	380
[ 3264 ] OspA-25015	340	350	360	370	380
[ 2802 ]. OspA-TRO	340	350	360	370	380
[ 2648 ] Ospa-K48	a. 340	tt	360	370	380
[ 2584 ]	c	ctt	<u>.</u>	••• ••• •••	c>
OspA-HE 11 [ 2580 ]		350 ctt		370	380 >
OspA-DK29 [ 2566 ]	340	350	360	370	380c .g.>
OspA-Ip90 [ 2562 ]		350	360	370	380 c .c.>
OspA-BO [ 2558 ]		350		370tg	
OSPA-IP3 [ 2558 ]	340 g	350	360 a a	370 ttg	380
OspA-PKO [ 2558 ]	340	350	360	370	380
OspA-ACAI [ 2556 ]	340	350	360	370tg	380 .

FIGURE 42 (7 of 16)

•						
ospa-P-GAU [ 2544 ]	340	.gt .	50 .ga	360 a	370 ttg	380>
	390	•	400	410	420	430
OspA-B31	AAA GGT TTT CCA	GAA GTA T CTT CAT A	CT GAA AAA AGA CTT TTT	ATA ATA ACA AC TAT TAT TOT TC	A GCA GAC T CGT CTG	GGA ACC AGA CCT TGG TCT
OspA-B31 [ 3288 ]	390		••••••	410	• • • • • • • • • • • • • • • • • • • •	
Ospa-Kā [3288]			400	410	420	430
OspA-N40 [ 3276 ]	390			410		430
OspA-ZS7 . [ 3264 ]	390			410		
OspA-25015 [ 2802 ]	390 c	t g	400	410 gg	420 a	430 t.>
OspA-TRO [ 2648 ]	390	t	400	410 .c ct	420 a	430 g>
OspA-K48 [ 2584 ]	390 g	ac	400	410 .c gt	420	430
OspA-HE 11 [ 2580 ]	390 g	a	400	410 .c gt	420	430
OspA-DK29 [ 2566 ]	390 g	ac	400	410 c gt	420 a.t .	430
OspA-Ip90 [ 2562 ]	390 g	c	400	410 c gt	420 a.t .	430
OspA-BO [ 2558 ]	390	t.g	400 c	410 ccg	420 .a. a.t .	430 a.>
OSPA-IP3 [ 2558 ]	390	t.g	400 c	410 ccg	420 .a. a.t .	430 a.>
OspA-PKO [ 2558 ]	390	t.g	400 c	410 ccg	420 .a. a.t .	430 a.>
Ospa-ACAI [ 2556 ]	390		400 c	410 ccg	420 .a. a.t .	430 a.>
ospA-P-GAU [ 2544 ]	390	t.g	400 c	410 ccg	420 .a. a.t .	430 a.>
	4	40	450 *	460	470	480
OspA-B31	CTT GAA	TAC ACA GO	A AAA TTA AE	GC GAT GGA TOT	GGA AAA G	CT AAA GAG

FIGURE 42 (8 of 16)

	GAA	CTT	ATG	lel '	CCT	TAA	TTT	TCG	CTA	CCT	AGA	ccı	TIT	CGA	TTT	CTC
OspA-B31 [ 3288 ]	• • •		440	•••	• • •	450		•••	4	60	•••		470 	•••	• • •	480 >
OspA-KA [ 3288 ]	•••	• • • •	440	•••		450	•••			60	•••		470	•••	···	480
Ospa-N40 [ 3276 ]			440	•••	.a.	450 •••	•••			60	•••		470 		•••	480
OspA-ZS7 [ 3264 ]	•••	•	140	•••	.a.	450 •••			4	60	• • •		470	•••	• • •	480
OspA-25015 [ 2802 ]			140	•••	•••	450 •••		• • •		60	c		470		• • •	480 a>
OspA-TRO [ 2648 ]			140	•••	.a.	450 a	•••				a.c		470			480 ده
OspA-K48 [ 2584 ]	•••		40	•••	.ac	450 a	•••			50	c		470		• • •	480 a>
OspA-HE 11 [ 2580 ]			140		.ac	450 a	•••			60 aa.		• • •	470		• • •	480 a>
OspA-DK29 [ 2566 ]			140		.ac	450 a				50	<u>,</u> c		470			480 a>
OspA-Ip90 [ 2562 ]			140	•••	.ac	450 a		•••		30 aa.	a.c		470	•••	• • •	480 a>
OspA-B0 [ 2558 ]	•••		140 t		.a.	450 • • g					a.c		170			480 a>
OSPA-IP3 [ 2558 ]	•••		140 t		.a.	450 ••g					a.c		170	• • •	<b></b>	480 a>
OspA-PKO [ 2558 ]	• • •		140 t	•••		450 ••9	•••				a.c		170	• • •		480 a>
Ospa-ACAI [ 2556 ]	•••		t	···	.a.	450 ••g	• • •	•••		0	a.c		170	• • •		480 >
ospA-P-GAU [ 2544 ]	•••		140 t		.a.	450 ••9			46				70			480 a>
			49	0		5	00			510			52	0		
OspA-B31	GTT CAA	TTA AAT	AAA TTT	CCC 222	TAT ATA	GTT CAA	CTT GAA	GAA CTT	GGA CCT	ACT TGA	CTA GAT	ACT TGA	GCT CGA	GAA . CTT	AAA TTT	ACA TGT
OspA-B31 [ 3288 ]		•••	49	0	•••		00			510	• • •		52	0	•••	>
OspA-KA [ 3288 ]	• •.•		49	0	•••		500			510	•••		52 	0	- • •	>

FIGURE 42 (9 of 16)

Ospa-N40 [ 3276 ]	•••	490	500	510	520
OspA-ZS7 [ 3264 ]	•••	490	500	510 t	520
OspA-2501 [ 2802 ]		490 aa	500	510	520 g>
OSDA-TRO	.c	490 at	500 c	510 g	520 cc>
OspA-K48 [ 2584 ]		490 at.	500 . ac	510 g	cgg 1 5201 530 c>
OspA-HE 11 [ 2580 ]		490 at.		510 g	cgg     520  530 c>
OspA-DK29 [ 2566 ]		490 at.		510	cgg ! 520! 530 c>
OspA-Ip90 [ 2562 ]	••••••	490 at.	500 .c,	510 • • • • • • • • • • • • • • • • • • •	cgg ! 520! 530
OspA-B0 [ 2558 ]	••• • • • • • • • • • • • • • • • • • •	490 aat.	500 ac	510 aa g g a	520 aat gt.>
OSPA-IP3 [ 2558 ]		490	500	510	520 nat gt.>
OspA-PKO [ 2558 ]		490	500	510	520
Ospa-ACAI [ 2556 ]		490	500	510	520 at gt.>
ospA-P-GAU [ 2544 ]	•	490		510	530
	530	540 *	550	560	570
OspA-B31	ACA TTG G	TG GTT AAA	GAA GGA ACT GTT CTT CCT TGA CAA	י אכיר אינה אכיר א	AA AAT ATT TCA
OspA-B31 [ 3288 ]	530	540	550	560	570
Ospa-ka	530	540	550	560	570
			*		

FIGURE 42 (10 of 16)

[ 3288 ]	• • • • • • • • • • • • • • • • • • • •	••• ••• •		••• ••• •••	••• ••• ••• •••
Ospa-N40 [ 3276 ]	530	• • •	550		570 ×
OspA-ZS7 [ 3264 ]	530	540			570>
OspA-25015 [ 2802 ]	530	540	550	<b>*</b>	570 g c.c>
OspA-TRO [ 2648 ]	530 aaa	540c.		560 gt	570 c.c c>
OspA-K48 [ 2584 ]	540 aaa	c	550 c	560- gt	570gct.>
OSPA-HE 11 [ 2580 ]	540 aaa		550	560	570gc>
OspA-DK29 [ 2566 ]	540	c	550 c	560 gt	570gct.>
OspA-Ip90 [ 2562 ]	540 a aaa	c	550 c	560	570 c.c>
OspA-B0 [ 2558 ]	530aa			- 560	570 g g.a g>
OSPA-IP3 [ 2558 ]	530aa	540	550	560	570 g g.a g>
OspA-PKO [ 2558 ]	530aa	540 a	550 c	560	570 g g.a g>
Ospa-ACAI [ 2556 ]			550 c		570 g g.a g>
ospa-P-GAU [ 2544 ]	530aa	540 a	550 c	560	570 g g.a g>
	580	590	600	610	620
OspA-B31			CA GTT GAA	CTT AAT GAC ACT	•
OspA-B31 [ 3288 ]	580	590	600	610	620
OspA-KA [ 3288 ]	580	590	600	610	620
OspA-N40 [ 3276 ]	580	590	600	610	620
OspA-ZS7 [ 3264 ]	580	590	600	610	620

FIGURE 42 (11 of 16)

			•		
OspA-2501 [ 2802 ]	5 580	590 aa a	600 .c	610	620 c. caa>
OspA-TRO [ 2648 ]	580 c	590 a a.a a	600 g	610 t a	620 tcc. cag>
Ospa-K48 [ 2584 ]	580	590 .	600	610	
OSDA-HE 11	1580	590 .	600	610	620 . tcg>
OSDA-DK29	580	590	600	610	•
Ospa-Ip90	580	590	600	610	620 .cc. cag>
OspA-BO [ 2558 ]	580	590	600	. 610	_
OSPA-IP3 [ 2558 ]	580	590	600	610	620 .cc. cag>
OspA-PKO [ 2558 ]	580-	590	600	610	
Ospa-acai [ 2556 ]	580	. 200	600		
ospA-P-GAU [ 2544 ]	- 580	590	600		620 .cc. cag>
OspA-B31	GCI ACI AAA	אאא ארדי הכיש הי	ראש הטעיע בייבאת הביי	660 CA GGC ACT TCA TCG TGA AGT	
OspA-B31 [ 3288 ]	630	640	650		
Ospa-ka [ 3288 ]	630	640	650		
Ospa-N40 [ 3276 ]	630	640	CED .		
Ospa-ZS7 [ 3264 ]	630	640	650	660	670
OspA-25015 [ 2802 ]	630	640 gg aa	650 a g g	660	670
OSPA-TRO [ 2648 ]	630	640	650	660 aatc	670

FIGURE 42 (12 of 16)

# SUBSTITUTE SHEET (RULE 26)

OspA-K48 [ 2584 ]	630	640 	650 aaa g	660 aaa	670 .c
OspA-HE 11 [ 2580 ]		640 t.c .g.	650 a.a g	660	670 t>
OSDA-DK29 [ 2566 ]	630	640	650	660	670 c >
OspA-Ip90 [ 2562 ]	630	640	650	660	670 c >
OspA-BO [ 2558 ]	630	640	650	660	670
OSPA-IP3 [ 2558 ]	630	640	650	660	670
OspA-PKO [ 2558 ]	630	640	650	660	670
OSDA-ACAI [ 2556 ]	630	640	650	660	670
ospA-P-GAU [ 2544 ]	630 <sub></sub>	640	650	660	670
	680	690		710	,
OspA-B31	ATT ACT GTA TAA TGA CAT	AAC AGT AAA . TIG TCA TIT	AAA ACT AAA GAO TTT TGA TTT CTO	. Catal care area	101
OspA-B31 [ 3288 ]	680	690	700	710	720
Ospa-ka [ 3288 ]	680	690	700	710	720
Ospa-N40 [ 3276 ]	680	690	700	710	<b>720</b>
OspA-ZS7 [ 3264 ]	680	690	700	710	720
OspA-25015 [ 2802 ]	680	690 ac	700 c.		
OspA-TRO [ 2648 ]	680	690		710	720
OspA-K48 [ 2584 ]	680	690	700 c a	710	720
OspA-HE 11 [ 2580 ]	680	690	700 c.a	710	720
Ospa-dk29	680	690	700	710	720

FIGURE 42 (13 of 16)

[ 2566 ] .	••••	gg	tç	с	• • •	c	•••	a	• • •	a	c	• • •	• • •	>
OspA-1p90 [ 2562 ]	68	gg	690 tc	cg.	•••	7( c	00	a	•••	710 a	c	•••	720 • • • •	>
OspA-B0 [ 2558 ]		680 gt		690	•••						710		•••	720 c>
OSPA-IP3 [ 2558 ]		680 gt		690 •••	•••	•••		00 c.a	•••		710	t	•••	720 c>
OspA-PKO [ 2558 ]		680 gt						00 c.a	•••		710	t	•••	720 c>
OspA-ACAI [ 2556 ]		680 gt	c	690		•••			• • •		710	t	•••	720 c>
ospa-P-GAU [ 2544 ]		680 gt .	c	690	•••	• • •	70 .c.	00 c.a	•••	•••	710	t	•••	720 c>
		730		7	40		•	750 *		*	76	50	_	
OspA-B31	AAC AC	CA ATT A	CA GTA	CAA GTT	CAA :	TAC	GAC	TCA	AAT	GGC	ACC	AAA	TTA AAT	GAG CTC
OspA-B31 [ 3288 ]	•••	730	)										• • •	>
OspA-KA [ 3288 ]	• • • • •	730	) 		40			750			76		• • •	>
OspA-N40 [ 3276 ]	• • • • •	730	• • • • •		40	• • •		750	• • •	•••	76 • • • •		• • •	>
OspA-ZS7 [ 3264 ]	•••••	730		• • •		• • •			• • •	•••	76 •••			>
OspA-25015 [ 2802 ]	g	730			40 a		• • •		gca	a	76		g	ِح <b>ة،</b> .
OspA-TRO [ 2648 ]	g	730					•	750			76	-	c	ده
OspA-K48 [ 2584 ]		730 a .	••••	740	a	• • •	750 •••	•••	gca	76 •••	0		7. C	
OspA-HE 11 [ 2580 ]		730	:		40 a.c .								c.,	a>
OspA-DK29 [ 2566 ]	g	730 a .		740	ag		750	•••	gca	76		t		70 a>
OspA-Ip90 [ 2562 ]	g	730 a .		740				•••	gca	76		t		70 a>
OspA-BO [ 2558 ]	g	730			40 a	• • •		750 c	gca	t ·	76 	0 t		a>

FIGURE 42 (14 of 16)

OSPA-IP3 [ 2558 ·]	g.,	730 a't		740 ·		750 .c gca	t	76	0 t	a>
Ospa-PKO [ 2558 ]	g	730 at	•••	740 . a		750 .c gca	t	76	0 t	ده
Ospa-ACAI [ 2556 ]	g	730 at	•••	740 . a	•••		t	•••	t	ده
ospa-P-GAU [ 2544 <sub>7</sub> ]		730 at	a.	740		750 c gca	t	76	t <sub>.</sub>	a>
	770	780	•	790	*	800		*	810	•
OspA-B31	CCC AGI	CCA CIT	GAA AT	T ACA AAA A TGT TTT	CTT C	eat gaa Ta ctt	TTA AAT	AAA TTT	AAC GCT TTG CGA	TTA AAT
OspA-B31 [ 3288 ]	770	780	• • • • •	790	•••	800	• • •		810	>
Ospa-Ka [ 3288 ]	770			790					810	>
Ospa-N40 [ 3276 ]	770	780		790		800			810	>
OspA-ZS7 [ 3264 ]	770	780		790 		800			810	>
OspA-25015 [ 2802 ]	770 c a	780 c	•••	790 ac.		800	c		810	>
OspA-TRO [ 2648 ]	c aac			ac.	•••		c		810	>
OspA-K48 [ 2584 ]	c aa.	780 c		790 c.	38 5	00 a.a	c	810	• • • • • • • • • • • • • • • • • • • •	>
OspA-HE 11 [ 2580 ]	770 c aa.	780 		790 c.	a	800 a.a	с	•••	810	>
OspA-DK29 [ 2566 ]	c aa			790 c.			с		• • • • • •	>
OspA-Ip90 [ 2562 ]	c aa			790 cg				810	g.t	>
OspA-B0 [ 2558 ]	770 c a.		· · · · · ·	790 ac.			c		810	>
OSPA-IP3 [ 2558 ]	770 c a.			790 ac.	•••	800	c	•••	810	>
Ospa-PKO [ 2558 ]	770 c a.	780		790 ac.	, •••	800	c	<i>:</i>	810	>

FIGURE 42 (15 of 16)

Ospa-ACAI [ 2556 ]	c a.	• • • • •	780 c	•••	•••	. 7 .a.	90 .c.	•••	800	c	• • •	810	• • •	g>
ospa-P-GAU [ 2544 ]	770 c a.	• • • • •	780 c	•••	•••		90 .c.	•••	800	c	•••	810	•••	>
· ·														
_	820 *					٠								
OspA-B31	AAA TA													
Ospa-B31 [ 3288 ]	820	.>								•				
Ospa-Ka [ 3288 ]	820	>						•						•
Ospa-N40 [ 3276 ]	820	>		-							,			
Ospa-ZS7 [ 3264 ]	820	>						•						
OspA-25015 [ 2802 ]	.g.>		•				-		\$1.5					
OspA-TRO [ 2648 ]	820					-								
Ospa-K48 8:	20	>												
OspA-HE 11 [ 2580 ]	820 >											•		
Ospa-DX29 82 [ 2566 ]	20	•												
OspA-Ip90 82 [ 2562 ]	20		_				•							
OspA-BO [ 2558 ]	820							,				-		
OSPA-IP3 [ 2558 ]	820													
OspA-PKO [ 2558 ]	820								•					
Ospa-ACAI [ 2556 ]	820													
ospA-P-GAU [ 2544 ]	820													•

FIGURE 42 (16 of 16)

	•											
_	.10			20			30				40	
ATG AAA A	AA TAT	TTA	TTG	# GGA	ATA	* GGT	CTA	ATA	TTA	ccc	* TTA	ATA
TAC TIT T	IT ATA	AAT	AAC	CCT	TAT	CCA	GAT	TAT	AAT	CGG	AAT	TAT
50	•	60 *		*		70	•		80		*	90
CCA TCT ALCCOR ACA TO	AG CAA IC GIT	AAT TTA	GTT CAA	AGC TCG	AGC TCG	CTT GAA	GAT CTA	GAA CTT	AAA TTT	AAT TTA	AGC TCG	GTT CAA
•	100		;	110		*	120			13	30	
TCA GTA QI AGT CAT C	ATT TA TAA AT	CCT GGA	GGT CCA	CCT CCT	ATG TAC	ACA TGT	GTT CAA	CTT GAA	GTA CAT	agt TCA	AAA TTT	GAA CTT
140	ŧ	150			10	50	•	:	170			180
AAA GAC AJ TTT CTG T	LA GAC MT CTG	GGT CCA	AAA TTT	TAC	agt TCA	CTA	GAG CTC	GCA CGT	ACA TGT	GTA CAT	GAC CTG	AAG TTC
•	190		2	200			210	-		22	0	
CTT GAG CT GAA CTC GI	AAA TT TTT AA	GGA CCT	act Tga	TCT AGA	GAT CTA	AAA TTT	AAC TTG	AAC TTG	GGT CCA	TCT AGA	GGA CCT	ACA TGT
230	•	240		•	2:	50·	_	:	260		_	270
CTT GAA GO GAA CTT CO	T GAA	AAA	ACT TGA	GAC	AAA	AGT	AAA	GTA	AAA	ATT	ACA	ATT
	280			290			300			31	_	****
GCT GAT G	CTA	* AGT	CAA	* ACT	AAA	TTT *	gaa	ATT	* TTC	444	# Gaa	ቀ ጥፋጋ
CGA CTA CT	rg gat	TCA	GTT	TGA	TTT.	AAA	CTT	TAA	AAG	TTT	CIT	CTA
320 *	•	330		*	34	*	*		350		•	360
COG TIT TO	ATT AT TAA TE	GTA CAT	TCA AGT	AAA TTT	AAA TTT	GTA CAT	ACC TGG	CTT GAA	AAA TTT	GAC CTG	AAG TTC	TCA AGT
*	370 *	*	3	80			390			40	0	
TCA ACA GA AGT TGT CT	LA GAA	AAA TTT	TTC AAG	AAC TTG	GAA CTT	AAG TTC	GGT CCA	GAA CTT	ACA TGT	TCT AGA	GAA CTT	AAA TTT
410	*	420		*	43	0		. 4	140		_	450
ACA ATA GI TGT TAT CA	CA AGA	GCA CGT	TAA	GGA CCT	ACC TGG	AGA	CTT GAA	GAA CTT	TAC	ACA TGT	GAC CTG	ATA TAT
	460			70			480			49	_	
AAA AGC GZ	LT GGA	TCC	GGA	AAA	GCT	AAA	GAA	GTT	TTA	AAA	GAC	TTT
TTT TCG CT	A CCT	AGG	CCT	TTT	CGA	TTT	CII	CAA	TAA	TTT	CTG	<b>ሕ</b> ኢአ
•	±	510		*	52	*	*		530		*.	540 *
ACT CTT GA	CT CCT	ACT TGA	CTA GAT	GCT CGA	GCT CGA	GAC CTG	CCG	AAA TTT	ACA TGT	aca TGT	TTG AAC	AAA TTT
•	550	_	5	560	•		570			58	:0	
GTT ACA GA	AA GGC	ACT	GTT	GTT	TTA	* AGC	AAG	AAC	* ATT	TTA	* AAA	TOC

Wednesday, April 27, 1994 11:37 AM

CAA TGT CTT CCG TGA CAA CAA AAT TCG TTC TTG TAA AAT TTT AGG

590 600 610 620 630

GGA GAA ATA ACA GTT GCA CTT GAT GAC TCT GAC ACT ACT CAG GCT
CCT CTT TAT TGT CAA CGT GAA CTA CTG AGA CTG TGA TGA GTC CGA

640 650 660 670

ACT AAA AAA ACT GGA AAA TGG GAT TCA AAT ACT TCC ACT TTA ACA TGA TTT TTT TGA CCT TTT ACC CTA AGT TTA TGA AGG TGA AAT TGT

680 690 700 710 720
ATT AGT GTG AAT AGC AAA AAA ACT AAA AAC ATT GTA TTT ACA AAA
TAA TCA CAC TTA TCG TIT TTT TGA TTT TTG TAA CAT AAA TGT TTT

CTT CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA
770 780 790 800 810

CTA GAA GGC AAC GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA GAT CTT CCG TTG CGT CAG CTT TAA TTT TGT GAA CTA CTT GAA TTT

820

AAC GCT TTA AAA TAG TTG CGA AAT TTT ATC

K48/Tro OBDA

Figure 43 (2 of 2)

10	20 30	40
ATG AAA AAA TAT TTA T TAC TTT TTT ATA AAT A	TIG GGA ATA GGT CTA AC CCT TAT CCA GAT	ATA TTA GCC TTA ATA TAT AAT CGG AAT TAT
50 60	70	80 90
GCA TGC AAG CAA AAT G	TIT AGC AGC CIT GAT CAA TOG TOG GAA CIA	GAA AAA AAC AGC GCT CTT TTT TTG TCG CGA
100	110 120	* * *
TCA GTA GAT TTG CCT C AGT CAT CTA AAC GGA C	CCA CTC TAC TIT CAA	CTT GTA AGT AAA GAA GAA CAT TCA TTT CTT
140 150	160	170 180
AAA GAC AAA GAC GGT A	AAG TAC AGT CTA AAG TTC ATG TCA GAT TTC	OCA ACA GTA GAC AAG CGT TGT CAT CTG TTC
190	200 210	220
ATT GAG CTA AAA GGA . TAA CTC GAT TTT CCT	ACT TOT GAT AAA GAO TGA AGA CTA TIT CTO	AAT GGT TCT GGA GTG TTA CCA AGA CCT CAC
230 240	250	260 270
CTT GAA GGT ACA AAA GAA CTT CCA TGT TTT	GAT GAC AAA AGT AAA CTA CTG TTT TCA TTT	COT TIT AAT TGT TAA
280	290 300	310
GCT GAC GAT CTA AGT CGA CTG CTA GAT TCA	AAA ACC ACA TTC GAN	A CTT TTA AAA GAA GAT F GAA AAT TTT CTT CTA
320 330	340	350 360
GGC AAA ACA TTA GTG CCG TTT TGT AAT CAC	TCA AGA AAA GTA AG AGT TCT TTT CAT TC	I TOT AGA GAC AAA ACA A AGA TOT CTG TIT TGI
370	380 39	0 400
TCA ACA GAT GAA ATG AGT TGT CTA CTT TAC	TIC AAT GAA AAA GG AAG TTA CTT TTI CC	T GAA TTG TCT GCA AAA A CTT AAC AGA CGT TTT
410 420	430	440 450
ACC ATG ACA AGA GAA TGG TAC TGT TCT CTT	AAT GGA ACC AAA CI TTA CCT TGG TTT GA	T GAA TAT ACA GAA ATG A CIT ATA TGT CIT TAC
450	470 48	490
AAA AGC GAT GGA ACC	G GGA AAA GCT AAA GE G CCT TTT CGA TTT C	TTT DAA AAA TTT TTD AAA TAC TTT TAA AAA TT
500 510	520	530 540
ACT CTT GAA GGA AAA TGA GAA CTT CCT TTT	A GTA GCT AAT GAT A I CAT CGA TTA CTA T	AA GTA ACA TTG GAA GTA TT CAT TGT AAC CTT CAT
550	* * *	70 580
AAA GAA GGA ACC CT	T ACT TTA AGT AAG G	AA ATT GCA AAA TCT GGA

. 2.

129/133

P-GAU/BO-OSPA Wednesday, April 27, 1996 11:22 AM

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA CGT TIT AGA CCT 600 620 GAA GTA ACA GTT GCT CTT AAT GAC ACT AAC ACT ACT CAG GCT ACT CTT CAT TGT CAA CGA GAA TTA CTG TGA TTG TGA TGA GTC CGA TGA 660 650 AAA AAA ACT GGC GCA TOG GAT TCA AAA ACT TCT ACT TTA ACA ATT TTT TTT TGA CCG CGT ACC CTA AGT TTT TGA AGA TGA AAT TGT TAA 710 700 690 720 AGT GTT AAC AGC AAA AAA ACT ACA CAA CTT GTG TTT ACT AAA CAA TCA CAA TTG TCG TTT TTT TGA TGT GTT GAA CAC AAA TGA TTT GTT 740 750 730 GAC ACA ATA ACT GTA CAA AAA TAC GAC TCC GCA GCT ACC AAT TTA CTG TGT TAT TGA CAT GTT TTT ATG CTG AGG CGT CCA TGG TTA AAT 790 770 780 GAA GGC ACA GCA GTC GAA ATT AAA ACA CTT GAT GAA CTT AAA AAC CTT CCG TGT CGT CAG CTT TAA TIT TGT GAA CTA CTT GAA TTT TTG

820

GCT TTA AAA TAG CGA AAT TTT ATC

Figure 44 (2 of 2)

	•	•		10		•	20			3(	)	•		40	
AT.	G AA C TT	A. T	AA/ TTI	ATA	TT. A AA'	A TI AA T	G GG	A AT	1 CC1	CIA CAI	ATA TAT	TTI	4 CCC	* TTA AAT	ATA A TAT
	50 ±			*	6	0 -			70			80			90
CC	A TG	T A	AAC	CAP GTT	AA A	I GI	AGC	AGC TCC	-	GAC	CTC	AA.	AAC	AGC	GTT CAA
				.00	•	•	110		•	120				30	
TC2 AG1	CA'	A T	GAT CTA	AAC	CC1	CCS CCS	GAA	ATC	AAA TTT	GTT CAA	CTT GAA	GTA CAT	AGC	AAA	CAA CTT
	140				150	)	4		.60	_		170			180
AAA TI'I	AA A	C . G	aaa TTT	CTC	GGC	. AAG	TAC	GAT CTA	CTA GAT	ATT TAA	GCA CGT	ACA TGT	GTA CAT	GAC CTG	AAG TTC
	*			90	•		200			210			_	20	,
CIT	GAC	3	CTT GAA	AAA	GCA	ACT TGA	TCT AGA	GAT CTA	AAA TTT	AAC TTG		GGA CCT	TCT	GGA CCT	GTA CAT
	230			*	240		•		50			260			270
CTT GAA	GA:	A (	CCC	GTA CAT	AAA	GCT CGA	GAC CTG	AAA TTT	×	AAA TTT	GTA CAT	AAA TTT	TTA AAT	ACA TGT	* TAA
	*		28	80	*		290			300			31	ro	
TCT AGA	GAC	3 (	gat Cta	CTA GAT	GGT CCA	CAA GTT	ACC TGG	ACA TGT	CTT GAA	~	GTT CAA	TTC AAG	AAA TTT	GAA	GAT CTA
	320				330		_		40			50			360
CCG	AAA TTT		aca Igt	CTA GAT	GTA	TCA AGT	AAA	AAA TTT	GTA- CAT	ACT TGA	TCC AGG	AAA TTT	GAC	AAG	TCA
	•		37				380			390			40		ng:
TCA AGT	ACA TGT		AAE TT	GAA CTT	AAA TTT	TTC AAG	AAT TTA	GAA CTT	AAA TTT	GGT CCA	GAA CIT	GTA CAT		*	AAA TTT
	410			*	420			43		_		40			450
ATA TAT	ATA TAT	7	ACA PGT	AGA TCT	GCA CGT	AAT TTA	GGA CCT	ACC TGG	AAA TTT	CTT	GAA CTT	* Tat Ata	ACA TGT	* GAA CTT	* ATG TAC
	*		46		*		70		•	480		ı.	49	0	
AAA TTT	AGC TCG	0	TA	GGA CCT	ACC TGG	GGA CCT	AAA TTT	GCT CGA	AAA TTT	CNA	GTT CAA	TTA AAT	AAA TTT	* AAG TTC	± TTT AAA
	500 *			*	510		•	52				30			540
ACT TGA	CTT GAA	0	AA: TT	GGA CCT	AAA TTT	GTA CAT	GCT CGA	AAT ATT	GAT CTA	AAA TTT	GTA CAT	aca Tot	TTG AAC	¢ GAA CTT	# GTA CAT
	*		55	_	*		60		•	570		_	58	0	
AAA	GAA	G	GA .	ACC	GIT	ACT		AGT	AAG	GAA	ATT	TCA	AAA	TCT	GGG

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> TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA CCC 620 630 GAA GIT TCA GIT GAA CIT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA 660 650 AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TIT TIT TGA CGT CGA ACC TTA AGT TIT TGA AGG TGA AAT TGT TAA 700 710 690 680 AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 750 740 730 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 800 780 770 GAA GOC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC

CTT CCG TIT CGT CAG CIT TAA TGT TGT GAA TIT CTT GAA TIT TTG

820 CCT TTA AAA TAA CGA AAT TTT ATT

Figure 45 (2 of 2)

		•		•	
•	10	20	•	30	40
AAA AAA TAC TTT TTT	TAT TTA ATA AAT	TTG GGA AAC CCT	ATA GGT TAT CCA	CTA ATA GAT TAT	TTA GCC TTA ATA AAT CGG AAT TAT
50	60	4	70		90
GCA TGC AAG CGT ACG TTC	CAA AAT GTT TTA	GTT AGC CAA TCG	AGC CTT	GAT GAA CTA CTT	AAA AAC AGC GCT TTT TTG TCG CGA
10	00	110	•	120	130
TCA GTA GAT AGT CAT CTA	TTG CCT AAC GGA	GGT GAG CCA CTC	ATG AAA TAC TTT	GTT CTT CAA GAA	GTA AGT AAA GAA CAT TCA TTT CTT
140	150	*	160	. 1	70 180
AAA GAC AAA	GAC GGT	AAG TAC	AGT CTA	AAG GCA	ACA GTA GAC AAG
			TCA GAT		TGT CAT CTG TTC
*	90	200	*	210	220
TAA CTC GAT	AAA GGA TTT CCT	ACT TCT TGA AGA	GAT AAA CTA TTT	GAC AAT	GGT TCT GGA GTG CCA AGA CCT CAC
230	240		250	, 2	60 270
CTT GAA GGT GAA CTT CCA	ACA AAA TGT TTT	GAT GAC CTA CTG	AAA AGT TTT TCA	AAA GCA TTT CGT	AAA TTA ACA ATT TTT AAT TGT TAA
2:	80	290	•	300	310
GCT GAC GAT CGA CTG CTA	CTA AGT GAT TCA	AAA ACC	ACA TTC TGT AAG	GAA CTT	TTA AAA GAA GAT AAT TTT CTT CTA
320	330		340	3	50 360
GGC AAA ACA CCG TTT TGT	TTA GTG AAT CAC	TCA AGA AGT TCT	AAA GTA TTT CAT	AGT TCT . TCA AGA	AGA GAC AAA ACA TCT CTG TTT TGT
	70	380		390	400
TCA ACA GAT AGT TGT CTA	GAA ATG	TTC AAT AAG TTA	GAA AAA CTT TTT	GGT GAA CCA CTT	TTG TCT GCA AAA AAC AGA CGT TTT
410	420	,	430	4	40 450
ACC ATG ACA	AGA GAA TCT CTT	AAT GGA TTA CCT	ACC AAA TGG TTT	CTT GAA	* * * TAT ACA GAA ATG ATA TGT CTT TAC
	60	470		480	490
AAA AGC GAT TIT TCG CTA	GGA ACC CCT TGG	GGA AAA CCT TTT	GCT AAA CGA TTT	GAA GTT CAA	* * * * TTA AAA AAG TTT AAT TTT TTC AAA
500	510		520		30 540
ACT CTT GAA TGA GAA CTT	GGA AAA CCT TTT	GTA GCT CAT CGA	AAT GAT TTA CTA	AAA GTA TTT CAT	* * * ACA TTG GAA GTA TGT AAC CTT CAT
	50	560		570	580
aaa gaa gga	ACC GTT	ACT TTA	AGT AAG	GAA ATT	TCA AAA TCT GGG

TIT CIT CCT TGG CAA TGA AAT TCA TTC CIT TAA AGT TIT AGA CCC GAA GTT TCA GTT GAA CTT AAT GAC ACT GAC AGT AGT GCT GCT ACT CTT CAA AGT CAA CTT GAA TTA CTG TGA CTG TCA TCA CGA CGA TGA AAA AAA ACT GCA GCT TGG AAT TCA AAA ACT TCC ACT TTA ACA ATT TTT TTT TGA CGT CGA ACC TTA AGT TTT TGA AGG TGA AAT TGT TAA AGT GTG AAT AGC CAA AAA ACC AAA AAC CTT GTA TTC ACA AAA GAA TCA CAC TTA TCG GTT TTT TGG TTT TTG GAA CAT AAG TGT TTT CTT 740 750 GAC ACA ATA ACA GTA CAA AAA TAC GAC TCA GCA GGC ACC AAT CTA CTG TGT TAT TGT CAT GTT TTT ATG CTG AGT CGT CCG TGG TTA GAT 790 800 770 780 810 GAA GGC AAA GCA GTC GAA ATT ACA ACA CTT AAA GAA CTT AAA AAC CTT CCG TTT CGT CAG CTT TAA TGT TGT GAA TTT CTT GAA TTT TTG OCT TTA AAA TAA CGA AAT TIT ATT

Figure 46 (2 of 2)

### INTERNATIONAL SEARCH REPORT

intel al Application No PCT/US 94/12352

A. CLASSIFICATION OF SUBJECT MATTER IPC 6 C12N15/31 C12N1 C12N15/62 C07K14/20 A61K39/02 G01N33/50 C07K16/12 According to International Patent Classification (IPC) or to both national classification and IPC **B. FIELDS SEARCHED** Minimum documentation searched (classification system followed by classification symbols) IPC 6 C07K C12N A61K G01N Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched Electronic data base consulted during the international search (name of data base and, where practical, search terms used) C. DOCUMENTS CONSIDERED TO BE RELEVANT Citation of document, with indication, where appropriate, of the relevant passages Relevant to claim No. X MOLECULAR MICROBIOLOGY, 1,6,7,9, 22,27, vol.6, no.20, 1992 pages 3031 - 3040 28,30,45 ROSA P. A. ET AL. 'Recombination between genes encoding major outer surface proteins A and B of Borrelia burgdorferi' see the whole document Further documents are listed in the continuation of box C. X Patent family members are listed in annex. X Special categories of cited documents: later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the document defining the general state of the art which is not considered to be of particular relevance earlier document but published on or after the international "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such docudocument referring to an oral disclosure, use, exhibition or ments, such combination being obvious to a person skilled in the art. document published prior to the international filing date but later than the priority date claimed "&" document member of the same patent family Date of the actual completion of the international search Date of mailing of the international search report n 3. 03. 95 24 February 1995 Name and mailing address of the ISA Authorized officer European Patent Office, P.B. 5818 Patentiaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Espen, J Fax: (+31-70) 340-3016

Form PCT/ISA/210 (second sheet) (July 1992)

Category , Cita	GINSBERG H. S. ET AL. (EDS.) 'Vaccines 93. Modern approaches to new vaccines including prevention of AIDS. Tenth annual meeting, Cold Spring Harbor, New York, USA, September 1992.' 1993, COLD SPRING HARBOR LABORATORY PRESS, NEW YORK cited in the application McGrath B. C. et al.: 'Biochemical and proper surface protein from north american and european isolates of Borrelia	 1-4, 10, 14, 17, 22-25, 31, 35, 38
O, X	GINSBERG H. S. ET AL. (EDS.) 'Vaccines 93.  Modern approaches to new vaccines including prevention of AIDS. Tenth annual meeting, Cold Spring Harbor, New York, USA, September 1992.'  1993, COLD SPRING HARBOR LABORATORY PRESS, NEW YORK cited in the application McGrath B. C. et al.: 'Biochemical and Diophysical characterization of the major outer surface protein from north american and european isolates of Borrelia	1-4,10, 14,17, 22-25,
	Modern approaches to new vaccines including prevention of AIDS. Tenth annual meeting, Cold Spring Harbor, New York, USA, September 1992.' 1993, COLD SPRING HARBOR LABORATORY PRESS, NEW YORK cited in the application McGrath B. C. et al.: 'Biochemical and biophysical characterization of the major outer surface protein from north american and european isolates of Borrelia	14,17, 22-25,
	ourgdorferi' see page 365 - page 370 see page 369, last paragraph	
F K a t	JOURNAL OF BACTERIOLOGY, vol.175, no.9, May 1993 bages 2516 - 2522 (ITTEN T. ET AL. 'Intragenic recombination and a chimeric outer membrane protein in the relapsing fever agent Borrelia nermsii' see the whole document	1,6-8, 22,27-29
A	VO,A,93 08306 (SYMBICOM AKTIEBOLAG) 29 April 1993 see claims 44-46	1-9, 22-30, 45-48
A	(O,A,91 13630 (THE UNITED STATES OF MERICA) 19 September 1991 see page 8; figures 11,13	1-9, 22-30, 45-48
1	O,A,94 20536 (THE REGENTS OF THE INIVERSITY OF CALIFORNIA) 15 September 994 see page 4-6; claim 6 	1,6,22, 27

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

### INTERMITIONAL SEARCH REPORT

Information on patent family members

Înteri	ıl Application No
PCT/	JS 94/12352

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO-A-9308306	29-04-93	AU-A- EP-A-	2903892 0540457	21-05-93 05-05-93
WO-A-9113630	19-09-91	AU-B- AU-A- CA-A- EP-A- JP-T-	645078 7496591 2077434 0524958 5501113	06-01-94 10-10-91 06-09-91 03-02-93 04-03-93
WO-A-9420536	15-09-94	AU-B-	6366894	26-09-94

Form PCT/ISA/218 (patent (amily annex) (July 1992)